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SOME ASPECTS OF INDUSTRIAL DERMATITIS*

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After the introduction of the Workmen's Compensation Act in 1906 industrial dermatitis became one of its largest causes of legal action. There very quickly arose the belief that "once a dermatitis always a dermatitis" was both true and unalterable. This belief is still blindly held by the majority of employers and employees as well as by far too many doctors. It has been encouraged by decisions in the courts, and Sir Edgar Dale wrote to me as follows: "I gathered that it was most unsatisfactory for any workman to return to the work at which he developed the disease, even after he had apparently recovered. He always seemed a subject prone to relapse. This was particularly so in a true industrial dermatitis of gradual onset due to long exposure. A sudden attack due to some specific irritant of course would recover and the man could return to his work if not subjected to the same irritant." He went on to repeat the old joke about prognosis in diseases of the skin, the joke best expressed by Belloc in his *Cautionary Tales*.

> Physicians of the utmost fame
> Were called at once; but when they came
> They answered as they took their fees,
> "There is no cure for this disease."

Since the last war, however, experience has shown that this belief has very little foundation in fact. The writings of Bettley, Pillsbury, Twiston Davies, and many others should be appreciated not only by dermatologists but by all medical practitioners concerned in this matter as well as by factory, education, and welfare officers.

Diagnosis

Our own difficulties have largely contributed to the layman's attitude, difficulties caused by the infinity of factors which can play a part in the development of an eczematoid eruption. Although certain external agents cause a reaction more commonly than do others, yet in fact it is probably true to say that any substance is a potential irritant to someone somewhere. Anything at all which is wrong with the general health can act as a debilitating factor and thus debilitate the skin so that it then reacts to an agent for the first time. Although repeated exposure can produce traumatic changes or sensitization it is more true that the rashes seen in older patients have not been caused solely by this exposure but rather by a change in the general health. With increasing age the skin also becomes drier and more atrophic, yet another factor in "long-continued exposure." Then there are the home and hobby contacts. The London Transport figures illustrate the importance of these in the high incidence of skin disease among the married women on the clerical staff. Thus the possibilities are unlimited, and obviously their relative importance cannot be assessed in five minutes, or even in five hours in many cases.

Add the unreliability of most histories as given by a patient who is usually not a trained observer, who is seen weeks or even months after the onset of the rash, whose reasoning is probably confined to *post hoc, ergo propter hoc*, whose opinions have been subjected to the views of his mates and his family—then we have a tangled web rivalling the most ingenious of "thrillers." In truth these histories are almost valueless except where they be factual.

It cannot therefore be surprising that our own doubts and difficulties have helped to confuse the layman. Far too often a busy surgery or a busy out-patient department allows a snap diagnosis or a false impression to be given. Even when the eruption is obviously that of some specific dermatosis, this may not be explained to the patient. In any case it is often extremely difficult to convince a cement-worker, for instance, that his rash is caused by an acarus and not by cement. We are well aware of these problems, but we do not or cannot always give the time and patience needed to gain the complete confidence of the victim. Even if we have been able to do this, there still remain the difficulties in handling the case of true industrial dermatitis. It is true that a man once labelled "dermatitis" often finds it almost impossible to obtain employment by other firms even at lower remuneration. Because of the fear of losing his job the man may well persist at work for weeks or months after the eruption first develops. Add to this the fear of contagion, for it seems to be generally believed that all skin diseases are in some way infectious. This view is encouraged by certification. Even where that particular fear does not exist, the condition is regarded as "dirty." Even Job (vii. 5) bewailed, "my skin is broken, and become loathsome." He may in fact be largely responsible for this view, for the Victorians quoted him with unremitting frequency.

Often a man has been carelessly told to avoid all future contact with dust. "Impossible" is the mildest term which can be applied to such an instruction. The delays of litigation may add to his troubles. These are but some of the problems which beset the man with dermatitis. Their importance cannot be minimized, but they should not be allowed to occur at all, for resentment can readily arise and can practically never be dispersed.

Incidence

First let us examine the figures given by the Ministry of Pensions and National Insurance, remembering, how-

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ever, that notification of industrial dermatitis is not compulsory and also that the figures are concerned only with working-days lost. Figures of the actual numbers of workmen concerned are not available. From Table I it is

TABLE I.—*Time Lost. Ministry of National Insurance Figures* for Twelve Months from June, 1953*

Total working days lost from all sickness and injury	300,290,000
Days lost on account of all skin diseases	4,030,000 (1·3%)
Days lost on account of industrial dermatitis (male 780,000, female 300,000)	1,080,000 (0·3%)

This represents 25,000 spells of incapacity due to industrial dermatitis. Numbers of individuals involved are not available.

Average duration of each spell .. .. Male 25 days, Female 35 days.

For various reasons, the Ministry figures are thought to cover but 85% of the working population.

seen that in fact all skin diseases account for only 1.3% of time lost through all incapacities; occupational dermatitis accounts for only 0.36% of total time lost. That figure is to me surprisingly low, yet it accounts for most of the compensatable industrial disease in Great Britain if there be excluded certain conditions mainly confined to miners. During the period from June, 1953, to June, 1954, some 1,080,000 days were lost, 780,000 being lost by men. This represents about 25,000 spells of incapacity. It is noteworthy that industrial dermatitis accounted for rather less than a quarter of all the skin diseases which compelled abstention from work. Further, it must be remembered that most dermatoses do not so incapacitate the patient that continuation at work is impossible. Therefore the actual proportion of industrial dermatitis must in fact be lower still.

This proportion must of course vary with the industrialization of particular areas. The position of King's College Hospital, in South London, is probably average in its relation to industry, to smaller suburban homes, and to somewhat better classes of property. Table II shows that, of 20,691 new cases seen in the skin department, 3,829 were cases of "eczema" in adults, about 18.5% of the total. Endogenous eczemas accounted for 10.5% of the total, exogenous eczemas for 6.5%, and industrial dermatitis for 1.7%. Of the exogenous cases industrial dermatitis represented only 26.2%.

Ellis (1946) has been chiefly concerned with chromate contacts, and he found that in the U.S.A. during 1944 and 1945, years of industrial stress, of the 2,500 employees exposed to chromates only 20 showed sensitivity—that is, only

TABLE II.—*Incidence at King's College Hospital*

Total Cases Reviewed	Total "Eczemas," Excluding Infants	Endogenous Eczemas Including Atopics	Seborrhoeic Eczema	Exogenous Eczemas of All Kinds	Industrial Dermatitis
20,691	3,829	2,178	296	1,355	356 (266 male)

TABLE III.—*Munition Work During the Stress Years of 1944–5 (Ellis, 1946)*

Period	Total Employees	Chromate Employees	Total Dermatoses	Total Chromate Reactions	Total True Industrial Dermatitis
2 years	10,000	2,500	235	20	60

1 in 250 per annum of these workers (Table III). Among 10,000 workers (including the above chromate contacts) there were 235 cases of dermatitis of all kinds but only 81 of these were occupational in origin; and even 21 of these 81 were due to dermatitis medicamentosa and other forms of post-traumatic dermatitis. Thus only about one-quarter of the dermatitis cases were occupational in origin. This figure agrees astonishingly with the 26.2% mentioned above.

Where factory conditions are of the best, the figures continue along much the same lines. Thompson reports that in a large factory averaging 12,500 employees there have been 5,746 cases of skin disease in 11 years. Of these, only 1,555 were industrial in origin—that is, an average of 141 cases a year. Among 12,500 employees that means that 1.15% suffered from a trade dermatitis. Of the skin cases treated at the works 20.1% were considered to be of industrial origin. Table IV shows very similar results in other efficient and large concerns. Bourne has found that about two-thirds of cases seen at one hospital emanated from small factories employing fewer than 200 hands.

The Ministry tables, of course, include all cases which have been certified. Most of these are not seen by a dermatologist until they have persisted for three months

TABLE IV.—*Incidence in Certain Groups. Figures Based on Personal Communications*

Employment	Average No. of Employees	Period Reviewed (in Years)	Average Annual Incidence of All Skin Diseases	Average Annual Incidence of Industrial Dermatitis	Annual No. of Cases where Permanent Change of Employment was Advisable
Car manufacture ..	12,500	11	522	141	7
National Coal Board (18 collieries) ..	18,027	5	—	88	—
Slough Group ..	17,000	10	441	42	—
Harlow Group ..	5,000	1½	—	18	Nil
Engineering ..	5,000	2½	77	10	"
Steel	8,940	2	574	27	"
Caterers	4,600	1	—	18	"
Wireless	2,369	1	76	19	"

TABLE V.—*Analysis of Cases Seen for the Ministry of National Insurance*

	No. of Cases			Found to be Non-occupational Dermatoses	
	Total	Males	Females	Males	Females
Sneddon ..	246	185 colliers	61	80	13
Thomson ..	370	282	88	76	18

That is, of the cases which have been accepted but which ultimately are reviewed by a dermatologist, about 30·3% were found to be non-occupational in origin.

and then come up for review. Of these, about 30% are then discovered to be non-industrial in origin if these available figures are truly representative (Table V).

In short, these considerations all confirm the view of industrial medical officers that dermatitis is not among their major problems.

The age incidence is obviously of very great importance and there is room for fuller investigation here. The London Transport figures are interesting, for although they are not concerned directly with occupational dermatitis they do show that men are mostly affected at or over middle age, whereas women show a low age-group incidence (Table VI). That is almost certainly explained by household chores. These points correspond with one's own impressions gained in out-patient departments, etc. Unfortunately it has not been possible to cover this aspect by the consideration of a very large number of cases.

TABLE VI.—*Age Incidence. London Transport Figures—Published in 1956. Skin Diseases are Dealt with only as "Infective" and "Non-infective" (International Code 690 to 698 and 700 to 716 Respectively). No Special Separation of Industrial Dermatitis*

Occupation	Total Exposure to Risk in Man-years	Days Lost Because of Non-infective Dermatitis	Conversion for Better Statistical Comparison	Greatest Age Incidence	Average Length of Spell Off-work (Days). (*Not* Complete Recovery Time)
Bus drivers ..	56,499	12,357	12,357	60–64	55·4
Male conductors	48,178	8,458	9,867	50–54	45·5
Motormen and guards ..	10,898	1,616	8,080	60–64	78·0
Male workshop staff	15,970	4,230	14,805	40–44	77·5
Clerical and technical staff	6,108	652	5,868	40–44	40·0
Clerical (unmarried women)	4,575	613	7,356	35–39	56·5
Clerical (married women) ..	1,933	465	13,485	30–34	43·8

Costs

The cost to the country in loss of time, loss of wages, payment of appropriate allowances, etc., can be calculated. It is more difficult to assess the loss to the workman, as this involves not only direct financial straits but the other features of distress caused by sickness and fear. The cost to the employer obviously varies with the nature of the work, but where special clothing, protective measures, washing facilities, etc., are provided, the information supplied to me assesses the average cost at about £12 per employee per annum. It has been impossible to get any idea of the cost in insurance. Several insurance companies have said that they work on overall risks and do not break down their figures into dermatitis, accident, etc. They do say that some smaller firms, being insured, seem to prefer to rely on their policies rather than make efforts to reduce the incidence. They also state that they encourage firms to keep disabled men on their books and do not in any way press for their dismissal, as has been suggested in some quarters.

Perhaps it is wrong to contemplate legal costs, and they certainly cannot be estimated. Table VII is of some interest, perhaps, in that it indicates my own experience as a result of such involvements.

TABLE VII.—*Court Attendances (Thomson). Cases Seen at the Request of Solicitors, Assessors, Trades Unions, Insurance Companies, and Employers*

1924 to 1949	1949 to 1957	Total
4,501	469	4,970
Court Attendances		
94 (2·08%)	27 (5·73%)	121 (2·43%)

Prognosis

Although the incidence of the disease is in fact quite low, the prognosis in these cases is one of the most important of considerations. It was the story of men forced to change their jobs, with consequent lower standards of living, and even of men incapacitated for life, that first suggested the subject for this lecture. How many of these stories are true? Inquiries of various Ministries, of insurance companies, of trade unions, of employers—all failed to produce any facts and figures. What evidence there is demonstrates that such cases must be few and far between. Sneddon has supplied information about rehabilitation which may be some guide. Out of 3,000 cases of the dermatitis-eczema group, only 47 were referred for resettlement. Of these, 33 were adequately dealt with by the disablement resettlement officer and only 13 had to go to a resettlement unit. There is no evidence regarding the numbers of these cases which were industrial in origin, but I think it fair to assume that less than one-third of them belonged to this category. On the other hand, he points out that the good workman finds himself a suitable job and bothers neither the D.R.O. nor the almoner. All the men agreed that to be put on the disabled persons register with skin disease increased the difficulty in getting work.

Most of us can remember only a handful, and all of these are suspect in that they seem to be either autophytic or other types of endogenous eczemas, although they were perhaps first detonated by a work contact. It is for this reason that Bettley suggested that a time limit be placed on the payments made to such cases. In Denmark compensation is given only in cases of chronic relapsing dermatitis, and then only to people working in certain trades or with certain substances defined in a special list published by the Board of Health Insurance.

The law is greatly concerned with prognosis, and Judge Alan Pugh regards this as the most important factor in the assessment of damage, because the claimant can bring only one action.

The differentiation between primary irritants and sensitizers, although not absolute, is gaining wider recognition, and to-day Calnan and others agree that only about 20% of these reactions have been caused by sensitizers. Hodgson has supplied figures for 263 cases which demonstrate that most prolonged damage is done by alkalis and by "detergents" when that term is used in its widest sense (Table VIII). His percentages are so striking that they must lend support to the belief that many dermatitis cases are aggravated or maintained by the compulsion to continue washing at work or at home, or as a result of imperfect instructions about treatment.

The Ministry of National Insurance lists about 60 different employments, and it is interesting to note the number of spells off work in various categories. The five largest and three small groups have been chosen as illustrations

TABLE VIII.—*Recovery Times (Hodgson)*

Complete recovery within 3 to 4 months occurred in:
80% of cases caused by primary irritants, excluding alkalis.
63% of cases caused by sensitizers.
9% of cases caused by alkalis.
5% of cases occurring in "wet" workers handling soaps and detergents.

TABLE IX.—*Dermatitis Cases Receiving Injury Benefit—Spells Terminating in* 1955

	All Spells	1st and Succeeding Spells							
		1st	2nd	3rd	4th	5th	6th	7th	8th
All occupations ..	20,967	18,258	2,214	382	74	23	9	5	2
Mining and quarrying	4,697	3,850	639	137	42	15	8	4	2
Personal service (i.e., hotels, clubs, institutions, etc.)	1,398	1,255	124	17	2				
Building	1,051	951	85	13	2				
Fitters	879	807	63	8	1				
Painters and decorators	536	459	65	11	1				
Alcoholic-drink makers	25	25							
Tobacco makers ..	10	10							
Musical-instrument makers	2	2							

(Table IX). Overall second attacks occur in only 10.5%. Miners head the list with more relapses than occur in any other occupation. This excludes tinea pedis, which is now compensatable in that calling. With them second spells occur in 13.6%. Among fitters this figure is 7.2%, in builders 8.1%, in painters 12.1%, and in those "engaged in personal service" 8.9%. This does not mean, of course, that about 90% of the affected workers change their jobs and that 10% remain at work to acquire second attacks. Rather does it mean that they learn by experience and thereafter take additional care. Thompson's experience leads him to believe that in fact only 5% do change their jobs.

A few quotations can now be introduced. Bourne says that "the healed industrial dermatitis patient is no greater risk than new personnel. A return to the old type of work with education and supervision and adequate protection will usually result in the work being carried out efficiently and without further difficulty." He is there speaking of epoxy resins and hardeners, to-day the greatest single source of contact dermatitis. Hellier states that "it is best never to put a man off work at all." Whittle's experience in medical appeal tribunals leads him to believe that "it is far better not to be certified in many cases because of bad effects on morale in particular." Crosthwaite finds that the vast majority of cases respond rapidly to treatment without absence from work or any change in occupation. Mackenna and Horner state that a man should be able to return to the job in cases of primary irritant contacts, after education and with preventive measures. They believe, too, that those who have reacted to sensitizers can be reintroduced to their work with care and supervision. Hodgson, however, believes that it is wiser to remove the workman from contact in acute cases caused by sensitizers.

Horner, discussing skin cancer hazards, states that the man who has thus suffered is in fact safer in returning to the same job because the hazard is there well recognized and the men have periodic examinations. This statement is so full of common sense that it is applicable, and should be applied, to all these cases. Sneddon thinks that machinists can always resume their original jobs after a few months'

alternative work, and also believes that "the average man, given the will to work, can recover from an attack of dermatitis and with some guidance can resettle himself adequately." The views of Twiston Davies on industrial dermatitis are too well known to require repetition here, but I must quote just one passage: "In this case the laws of Nature are suspended, and all that we may think we know, by experience and scientific investigation of allergy, must be forgotten."

There are yet other factors in considering the possibility of relapse. To believe that "once a dermatitis always a dermatitis" is to believe in an irreversible change, and this is unsupported by evidence. There is, too, the view that an attack caused by one agent invariably renders the skin more liable to damage by any other agent. Calnan, Wilson, Twiston Davies, and others have all indicated that such polysensitization is rare except in chemically related substances.

Plurality of causation factors does not occur in that way, but is found in the other agents which are present mostly in the middle-aged and elderly. In the same way plurality of maintenance factors can occur in any patients; general ill-health, toxic foci, overtime, home remedies, loss of earnings, home conditions, fears accentuated by wrong diagnosis, wrong advice, and unsympathetic handling are only some of these bad influences. Friction and scratching are potent in this way, even after all rash has disappeared. This then occurs simply because the eruption lowered the itch threshold of appreciation, so that thereafter the patient is unduly conscious of the normal physiological itching which is always present in everybody. Incidentally I have found that the easiest way to stop friction, etc., at this stage is to use a 1% brilliant-green ointment, the nuisance of which is most corrective.

The longer the man is off work the harder it is to get him back to work. On the other hand, men often return too soon, either because they are good and keen workers or because of financial stringency. This may militate against complete recovery, for, the longer the contact with the agent continues after the development of signs and symptoms, the slower the healing and the greater the risk of recurrence. The same effect is achieved by those who loathe going to their doctor and do not do so until the condition is obscured by treatment by themselves or by a firm's nurse. Blonstein further points out that others are resentful because they are not allowed to work when the condition first appears, and once it is established they are treated as pariahs.

In spite of all these besetting difficulties there remains the general opinion that but little industrial dermatitis causes real disability. On the very rare occasions when this does occur—and that seems to be in only about 1%—it is very disabling and intractable. While these numbers are relatively small, we should be able to reduce them to a great extent and, equally important, we should be able to eliminate the sense of impotence and that "sad patience, too near neighbour to Despair." To this end some reminders and some suggestions are reviewed.

Education

"What is needed is morale, not only the personal morale of the workman but pride in his work and confidence in the management, and a lot less of uninstructed contemplation of the human integument and its ills." Many of us have the greatest sympathy with this view, expressed so often by Twiston Davies; for there is no doubt that the Welfare State has diminished the sense of personal responsibility in many places. For this reason some education of the workman must be undertaken, but education must not be restricted to him.

First we must put our own house in order and try to appreciate all the difficulties of diagnosis and treatment, extending our knowledge to the harassed general practitioner and co-operating far more with the industrial medical officers. Their achievements are not appreciated enough; but their numbers are far too small, for at present only the large firms can use their services efficiently. A real advance can be made if the smaller factories are grouped into districts for supervision. Education officers could work, too, in these groups. Thus some imitation of the Slough and Harlow schemes could be achieved in the older towns. The skin departments of hospitals could be brought into closer contact and could be used more freely as consultation centres to the benefit of all concerned. The unfortunate undergraduate already has far too much ground to cover, but, just as one or two lectures on tropical diseases serve both as a change and as an interesting tonic, so could industrial medicine be introduced. Recruits to this branch might then readily be forthcoming. Perhaps this point has not been considered by those who estimate the numbers of medical practitioners who will be necessary in years to come. This subject should also play some part in post-graduate courses, and indeed the Institute of Dermatology is already trying to develop a special department and to integrate research in conjunction with the industrial medical officers of the London group.

TABLE X.—*Factories Employing Medical Practitioners and/or Nurses (Total Number of Factories Reviewed, 21,693)*

Medical officers are employed:	Nurses are employed:
Whole-time at 421 factories.	Whole time at 4,437 factories.
Part time:	Part-time at 642 factories.
Over 12 hours weekly at 252 factories.	None employed at 16,614 factories.
Under 12 hours weekly at 3,946 factories.	Persons with some nursing training employed at 4,432 factories.
None employed at 17,074 factories.	

Bourne found that 66% of industrial dermatitis came from small factories employing fewer than 200.

It is difficult indeed to give more time to these individuals in out-patient departments, but efforts along these lines must be made, not only to elucidate the problems but also to gain the confidence of the patient in the diagnosis. At present the somewhat brusque rejection of a claim for industrial injury benefit makes no difference whatever to the patient's belief that he is suffering from industrial dermatitis. It is disturbing but not surprising to discover how many laymen are willing to instruct us in this most difficult problem.

Many factories employ nurses only and do not appreciate the fact that they are not qualified as doctors. Whilst the value of their services in giving first aid, doing dressings, etc., is freely and gratefully acknowledged, yet many are encouraged to give advice on subjects outside their immediate scope. Far too often is one told that a nurse has diagnosed industrial dermatitis and has then proceeded to tell the man that he must stop work at once and must change his employment permanently. Many practitioners of course do the same thing on insufficient evidence. This brings us back to the need for more industrial medical officers with their specialized knowledge of processes and chemicals involved; men who can really advise employers and who can accept the responsibility which should be delegated to them.

Employers often find themselves in grave difficulties. Factory inspectors can only draw attention to and instruct on legal requirements of Factory Acts and Codes of Regulations. They can only recommend on these points. Only in certain dangerous trades is it in fact a legal requirement for a firm to have a doctor, but the Minister has retained the power to appoint one in any particular factory for a particular reason. Although firms are taking more and more trouble to check possible dangers in new processes, there is still no statutory requirement for them to do so. Nevertheless the two following legal decisions cannot be too widely known.

The first concerns the additional duty imposed upon the employer to take safeguards when he knows of the sensitivity of his worker, following the judgment of the House of Lords in the case of *Paris* v. *Stepney Borough Council*; the other is the decision of the Court of Appeal in *Clifford* v. *Chalen*, in which the employers were held to be negligent when, having made a barrier cream available, they did not take any special steps to see that their workers used it. Mention is made of barrier creams in the latter case and

great stress is laid on its use. Yet the value of barrier creams must still largely remain *sub judice*, for many experienced dermatologists regard them as most valuable and capable of development along specified lines, whilst many others think their chief value lies in their ability to facilitate washing. A similar divergence of opinion concerns the official placards which are provided for exhibition in factories. Many regard their presence as being actually harmful in that they constantly remind the workman of his skin.

The real secret of success lies in the happy relationship with labour, here as in everything else, but which must involve give and take. Small firms should try to adapt the methods of their larger and richer brothers who consult the appropriate employees during the development of new processes, etc. They could also with advantage often consult them before new buildings are constructed. Most of us have seen hospital plans which can only be described as fantastic in their inconvenience. Automation now offers great opportunities to extend the "no-touch technique." At a recent meeting of the Ergonomics Research Society, Burger said that "the automatic factory must also be safe. All too often industrial medicine is a forgotten factor, and the industrial physician must be asked to co-operate with designer and ergonomist."

It would be helpful if makers of oils, cleansers, etc., were compelled to print the compositions of their products on the containers, as in the case of patent medicines.

The policy of looking after employees should be universal. Someone more responsible than a shop steward should be in charge of safety precautions. Any necessary temporary or permanent change of employment is achieved by large concerns. It could be carried out in the area unit suggested, with the help of the local Labour Office, the D.R.O., and the National Insurance Office. This should be a part of their duties.

The first point in the education of the workman is to convince him that his welfare is under consideration. In the prevention of dermatitis the really essential factor is cleanliness—cleanliness of method, machine, person, and clothing. Hawton makes the cautious remark that "personal hygiene . . . proves to be tedious to some people and they are inclined to rush it or to shirk it altogether." This is all too true, and attempts to encourage cleanliness have been met by active resentment or lack of co-operation. In one large factory wash-basins were repeatedly smashed and lead piping was stolen. By constant replacements the employers have at last induced their acceptance and use. In another firm hot-water supplies were persistently allowed to run to waste. Cloth towels often seem to dissolve as readily as soap.

This difficult subject requires persistence, tact, and diplomacy; but, if cleanliness were general and thorough, the incidence of industrial dermatitis would be decreased enormously. It is, for instance, quite astonishing in these days to realize that about 1 in 1,000 juveniles are rejected at their first examination because of pediculosis (Table XI). Just occasionally scruffiness can serve a purpose. One man who worked in an atmosphere containing minute traces of a deleterious vapour found that he could avoid irritation of the face by shaving at the end of the day's work, the stubble having been protective.

Education officers do teach safety precautions, but technical schools and colleges could easily instil the idea of real cleanliness into their pupils. Trevethick believes that one of the best features resulting from National Service is found in the fact that these young men have learnt the value and acquired the habit of cleanliness.

This is not the place or time to discuss treatment except to stress the value of final dressings just before a man leaves work. The job has been done properly, and it allows him to return home without having to contemplate the domestic difficulties which sometimes accompany home dressings. A final plea can be made for skin departments generally. They should have sufficient whole-time staff to undertake the routine daily dressings for most dermatoses. The efficiency of such an arrangement halves the time required for healing to take place. The consequent saving to the patient, to the employer, and to the country would quickly justify the original increase in the cost of the department.

TABLE XI.—*Rejections Among 509,620 Juveniles*

	Rejected		
	Male	Female	Total
Total	588	1,090	1,678
Rejected because of skin diseases ..	42	86	128
Rejected because of pediculosis ..	16	501	517

Conclusion

A diagnosis of "dermatitis," often unnecessarily and at times incorrectly made, can at present damn a working-man for all time. This need never occur. May I therefore conclude with a quotation from Bettley: "Any man with a chronic eczema which interferes with his work is in an unhappy position; but his lot is not improved by unnecessary idleness, and he should be encouraged to continue suitable work, I mean actual work, not as night-watchman. If, on the other hand, he is given the benefit of the doubt and certified industrial, he will probably stop work altogether and may deteriorate. . . . There is no 'benefit' of this doubt."

Very many of my colleagues have given freely of their help, as have many laymen. It is not possible to acknowledge my debt to many personal communications. To all I express my very real thanks.

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OESOPHAGEAL ATRESIA

EXPERIENCE IN 17 CASES, WITH NOTES ON OPERATIVE TECHNIQUE

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Though, according to Mackenzie (1884), congenital atresia of the oesophagus was recognized by Dursten as long ago as 1670, no surgical success was recorded until 1939, when Leven (1941) and Ladd (1944), working independently of each other, performed multiple-stage operations for this condition, with survivals. These were followed two years later by the first successful end-to-end anastomosis by Haight (Haight and Towsley, 1943).

The history of the events leading up to these successes has been very adequately described by Leven *et al.* (1952), who discussed the various unsuccessful methods, such as gastrostomy alone, jejunostomy, etc., which were tried prior to 1939, and described their experiences in 103 cases occurring between 1939 and 1952. The operations in their series were performed by nine different surgeons. That large series of cases, and a few other series such as those of Gross (1953), who reports 233 cases, and Haight (1952) with 131, are quite exceptional and will not nearly be approached by the great majority of thoracic surgeons who have the responsibility of treating this condition.

No really large series has been reported from this country, but if one accepts as correct the estimate of Belsey and Donnison (1950) that congenital atresia of the oesophagus occurs once in every 800 births, then some 600 children so afflicted are born every year in the British Isles.

Diagnosis

The diagnosis of this condition has been discussed in detail by many authors (Lanman, 1940; Ladd, 1944; Flett *et al.*, 1949; Leven *et al.*, 1952; d'Abreu, 1953; Grow and Neerken, 1953; Koop *et al.*, 1954; Clatworthy, 1955; Nicks and Caughey, 1955; Roberts *et al.*, 1955), but the most important point is to be aware of it. The symptoms are fairly constant, and, in brief, the condition should be suspected in any newborn child who shows difficulty with respiration, excess mucus secretion, choking or intermittent cyanotic attacks, or who has a maternal history of hydramnios. These symptoms are often precipitated or accentuated when feeding is attempted.

Confirmation can easily be obtained by passing a size-8 well-lubricated urethral catheter down the oesophagus. Clatworthy (1955) makes the point that it should be passed through the nose, whence in normal infants it will enter the stomach easily (proved by the auscultation of injected air or by epigastric palpation), whereas in an infant with oesophageal atresia it will be held up 10 to 15 cm. from the tip of the nose.

Radiological confirmation by the instillation of lipiodol into the upper pouch is not a diagnostic necessity and carries the additional hazard of spill-over into the bronchial tree. If, however, it is undertaken, only a few drops of radio-opaque medium are necessary, and these should be instilled under fluoroscopic control and aspirated immediately the film has been taken.

Diagnosis of the much rarer tracheo-oesophageal fistula without atresia is difficult, and Koop *et al.* (1954) mention two such cases; one was seen by the bronchoscopist, and the other was found when the No. 10 catheter in the stomach was withdrawn and respiratory sounds were heard as the end passed the fistula. This condition should be suspected if intermittent symptoms persist after a catheter has confirmed the absence of atresia.

The earlier the diagnosis is made, the greater the chance there is that surgery will be successful. Koop *et al.*, in their series of 61 cases, noted a 46% mortality rate in the cases operated on before 72 hours and a 75% rate in three operated upon after this time.

In our series of 17 cases (10 females, 7 males) only one patient was operated on after 72 hours, and he survived; but, paradoxically, we found the average time between birth and operation in the survivors was 47 hours, while in the non-survivors it was 39 hours; these figures, however, include deaths from other associated conditions which in themselves were lethal. The earliest diagnosis in our series was 1½ hours after birth, and was made by a midwife who was endeavouring to administer intragastric oxygen.

TABLE I.—*Results*

Case No.	Birth Date	Sex	Type of Anomaly	Operation	Remarks
1	2/10/51	F	1	Usual extra-pleural	Died 2nd post-op. day from tension pneumothorax
2	2/11/51	M	1	,, ,,	Good, alive and well
3	11/10/52	M	1	Usual trans-pleural	,, ,,
4	29/10/52	F	1	,, ,,	Needed intermittent dilatation for 2 yrs. Now swallowing well
5	19/11/53	M	1	Unfit	No operation. Died 3rd day
6	14/12/53	F	1	Usual trans-pleural	Congenitally deaf. Stricture excision
7	15/5/54	F	1	,, ,,	Died 5 hours post-op. Had gross cardiac defects
8	4/6/54	F	2a	Gastrostomy. No anastomosis possible	Died 3rd post-op. day. Collapsed lower lobe
9	1/8/54	F	1	Usual trans-pleural	Good; alive and well
10	10/9/54	M	1	,, ,,	,, ,,
11	9/11/54	F	1	,, ,,	Died 4th post-op. day. Pneumothorax
12	19/3/55	M	1	,, ,,	Died 4th post-op. day. Congenital scleroedema
13	3/7/55	F	1	,, ,,	Had needed intermittent dilatation
14	19/9/55	F	1	,, ,,	Died 8th post-op. day. Empyema. Necrosed oesophageal wall
15	7/3/56	M	1	No operation	Diagnosed at necropsy. 2nd day after birth.
16	26/6/56	F	1	Usual trans-pleural	Has gastrostomy and needs occasional dilatation
17	6/9/56	M	1	Usual trans-pleural plus a transverse colostomy for imperforate anus	Good, alive and well. Imperforate anus subsequently repaired and colostomy closed

Other Congenital Anomalies.—It is a well-recognized fact that oesophageal atresia is often associated with other congenital anomalies (Leven *et al.*, 1952; Koop *et al.*, 1954; Clatworthy, 1955; Nicks and Caughey, 1955), and not infrequently these may be gross, multiple, and incompatible with life. It would seem that a genetic factor can be present in one parent. Mackenzie (1884) cited a case of a father, all of whose children by three wives showed this anomaly; and Sloan and Haight (1956) reported the occurrence of oesophageal atresia in brothers. One of our patients had a sibling with atresia of the oesophagus, and the mother of these children had webbed toes. In our series of 17 cases five children had other congenital abnormalities, of which two were gross—one having a cleft-palate, an atrial septal defect, a ventricular septal defect, and persistent ductus arteriosus, and the other having an imperforate anus, thoracic hemivertebra, and bilateral inguinal herniae. One child had a Meckel's diverticulum, one had congenital duodenal atresia, and one was completely deaf.

Obstetric History

Twelve of these patients were first babies, two were second, and three were third. One of the last was the

smallest of triplets. Four of the babies were born between 37 weeks and term and the remainder at full term. Four of the mothers were reported to have hydramnios, two toxaemia of pregnancy, one an ante-partum haemorrhage, and one a threatened abortion at 20 weeks. Hydramnios was noted by Clatworthy (1955) in 3 of his 35 cases, and its association with oesophageal atresia is also remarked upon by Nicks and Caughey (1955). Scott and Wilson (1957) found hydramnios in 12 out of 13 cases in their series.

According to Leven (1941) separation of the primitive foregut into trachea and oesophagus is usually present in the 8-mm. embryo; and Gruenwall (1940), who found oesophageal atresia and tracheo-oesophageal fistula in a 9-mm. human embryo, explains the condition as a failure of separation.

Various classifications of the condition have appeared in the literature. That of Vogt (1929), which is often quoted in papers on this subject, does not sufficiently emphasize the frequency of the commonest variety. Gross (1953) described six main groups, and Roberts *et al.* (1955) further subdivided the commonest group into those where the fistula enters the bifurcation low down, with a considerable length of atretic segment, and those where it enters the trachea high up, with overlapping of the fistula by the upper pouch.

It would seem of value to divide the cases into two main groups—those where a primary anastomosis can be performed (Group I) and those where anastomosis is impossible (Group 2a) or unnecessary (Group 2b), ligation of the fistula being all that is required (see Diagrams).

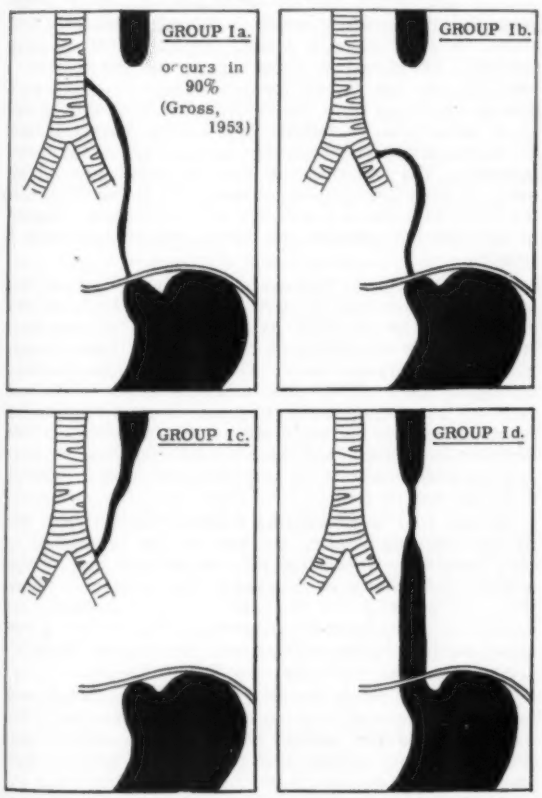

FIG. 1.—Group 1a: Atresia of the upper segment with lower oesophagus making fistulous connexion with the trachea. Group 1b: Same as 1a, but the fistula is either to the bifurcation of the trachea or to the left main bronchus. Group 1c: The upper oesophageal segment has a fistulous connexion with the trachea or the bifurcation. The lower segment of the oesophagus is a short, blind stump at the diaphragm. Group 1d: There is a narrowing of the oesophagus (or even a complete atresia) at a point near the tracheal bifurcation, but no fistula is present. Various combinations and permutations of these varieties may occur.

In our series 16 (94%) were in group 1, and three of these had the sac and fistula in contiguity. One case in this group had a very high take-off of the lower end, the origin being only just below the vocal cords. Two of the group had a band from the trachea for a few millimetres before it opened out into the lower oesophagus. One case was a Group 2a variety.

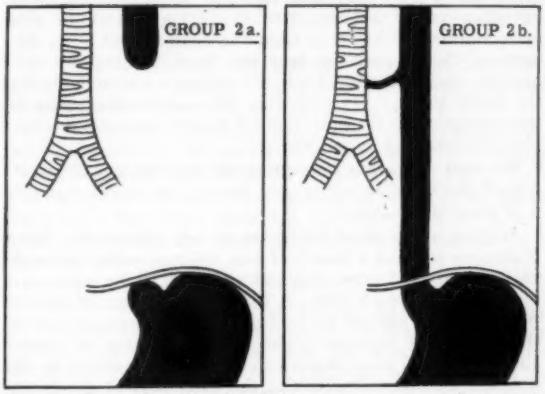

FIG. 2.—Group 2a: Atresia of the upper oesophageal segment and an absent lower oesophageal segment. Group 2b: A fistulous connexion between the oesophagus and the trachea. Adults with this variety have occasionally been reported, no operation having been performed.

The Operation

Pre-operative Preparation.—Time spent on improving the general condition is good up to a point, and we are very much in agreement with Clatworthy (1955), who believes that one rarely gains by devoting more than 12 hours to this; in fact, if the infant's condition is so poor that he cannot be prepared in this time there is little hope of salvage. While Nicks and Caughey (1955) have remarked that operation in the early hours of the morning with a skeleton staff probably carries a greater risk than if it is done early the next day, this has not been our experience. In fact, we feel that in a busy general hospital, where lists are often scheduled throughout the day, the night offers uninterrupted operating time which otherwise may not be easily available. In addition, the full and willing co-operation of the anaesthetic and paediatric teams has always been obtained on these occasions.

Aims of the Operation.—The ideal to aim at is closure of the tracheo-oesophageal fistula when present and anastomosis of the two ends of the oesophagus at one operation. The following description applies to those cases where this apposition is feasible. The treatment of the others is discussed later. The operative details of the condition have been discussed fully by many of the authors previously quoted, but the following description contains a number of points which do not seem to have been mentioned hitherto and which we feel are of great importance if a successful result is to be attained. An intravenous cut-down transfusion, using "polythene" tubing into a saphenous vein, is set up in the ward and 1/200 gr. (0.32 mg.) of atropine is given three-quarters of an hour before the operation is due to start. The infant is grouped and 1 pint (570 ml.) of blood is cross-matched; but great caution must be used in its administration, and the amount given in our series varied between 40 and 70 ml.

Anaesthetic

The anaesthetic consists of nitrous oxide at 3 litres a minute, oxygen at 2 litres a minute, and "tubarine," 2 mg. per stone (0.3 mg. per kg.), or suxamethonium chloride, 6 mg. per stone (0.94 mg. per kg.) initially. A further dose of 0.5 mg. of tubarine or the equivalent is given as required.

A Magill size 00 armoured endotracheal tube is passed and connected to an M.I.E. infant absorber, and the anaes-

thetist has available lengths of No. 2 size polythene tubing for frequent suction throughout the operation. It is advisable to mark off the length of the Magill tube on the polythene tubing with a small piece of sticking-plaster before the anaesthetic is started, and to round off the end of the tubing by holding it momentarily in a flame.

Frequent suction of the bronchial tree throughout the procedure is most important, not only to remove secretions but also, as we discovered in one of our cases, to give early warning of bleeding from the ligated fistula. In this instance the anaesthetist had not been sucking out frequently, and noticed difficulty in inflating the lung during the latter stages. On removing the endotracheal tube at the conclusion of the operation he found it was almost completely filled with blood clot.

We used diathermy for cutting the muscles and coagulating all the bleeding-points, and there is no doubt that this is a great time-saver.

Position.—The child is laid on its left side on the damp diathermy pad and a length of 4-in. (10-cm.) wide zinc oxide plaster is applied across the hips and fixed to the under part of the table on each side. A further small piece of narrow plaster is then applied to the flexor and extensor surfaces of the uppermost forearm (right), leaving a loop of plaster some 12 in. (30 cm.) long which can be manipulated by the anaesthetist or a nurse during the early part of the operation, when scapular retraction is required.

Instruments

Special instruments for these cases greatly facilitate the operation. Firstly, the very small space available in which to work demands a thoracotomy retractor which lies out of the way and at the same time gives adequate exposure. One of us has designed such an instrument (Cummins, 1954).

Secondly, the Tudor Edwards infant rib shears are very useful for the rib resection, but a strong pair of heavy scissors are quite effective for this purpose, and can be used if the shears are not available.

Thirdly, the smallest type of skin hook is an essential to atraumatic handling of the very delicate tissues. We use the kind designed by Gillies. These are particularly useful during the anastomosis, as the long handles enable the assistant to keep his hands well away from the wound while at the same time anchoring either end of the oesophagus securely.

Fourthly, a suitable needle-holder must be available; any cross-action variety, such as Mayo's in which the thumb and forefinger pass through the ring handles, is far too clumsy, and tearing of the tissues can occur when the needle is released. We have found that Silcock's ophthalmic needle-holder is an excellent instrument for the purpose, as the self-locking device enables the operator to hold it between finger and thumb, as one would a pen.

Fifthly, a long-handled pair of non-toothed dissecting forceps and a small edition of a right-angled artery forceps, such as those of O'Shaughnessy, also with long handles, are most useful for the dissection.

Finally, the sutures for the anastomosis and the fistula must be atraumatic, and we have found that 5.0 black braided silk arterial sutures (Ethicon code No. 595) answer the purpose very well.

Procedure

An oblique incision is made through the right chest, and after the muscles have been divided in the line of the incision a suitable rib, usually the fourth, is resected subperiosteally and the pleural cavity entered through the rib bed. We prefer this to an intercostal incision because of the greater ease with which the chest can be closed.

An extrapleural approach was used in the first two cases in this series, but subsequently we have used the transpleural. We feel that the theoretical advantage of the former in localizing a suture-line leak and possibly avoiding an empyema is more than offset by the extra time taken to dissect this very fragile tissue. With the transpleural approach, the parietal pleura over the oesophagus needs to be incised, and with a careful technique a watertight closure of this can usually be obtained on completion of the anastomosis.

The azygos vein is divided between ligatures, and the ends of the oesophagus are sought and mobilized.

The first essential is the closure of the fistula where one is present, as in a few of our cases the anaesthetist was embarrassed by the inflation of the stomach which occurred during the manual compression of the bag before this closure was completed. Early mobilization of the lower segment and slight tension upon a tape passed around it will prevent this happening.

The lower oesophagus must be cut off almost flush with the trachea and a careful closure made by interrupted sutures. This can be subsequently reinforced, if necessary, by available contiguous tissue or a free muscle graft. If a fistula is not present the lower segment is trimmed back by the removal of serial thin slices until the lumen is reached and the cut end bleeds freely.

A size 8 soft rubber urethral catheter passed down into the upper pouch by the anaesthetist is a help in mobilization of the upper pouch, but when working by touch under the sterile towel it often bends and will not enter the pouch easily. However, a size 1 Magill tube, cut off so that it is about 4 in. (10 cm.) long and passed alongside the endotracheal tube at the time of intubation, is a most useful guide for the catheter, which is threaded down it and allows its easy insertion without bending at the critical moment. The dissection of the upper pouch can be greatly aided by the use of two traction sutures on either side near the end, and when this mobilization is completed the tip is incised and the catheter drawn down through it into the wound and threaded into the cut open end of the lower segment. The two ends can then be gently opposed by manipulation of the traction sutures and of skin hooks in the lower end, and any appreciable gap assessed. It may be necessary to mobilize still further before commencing suturing.

A discrepancy in thickness of the two ends is not unusual, and, in fact, we have often been struck by the very poor tissue of which the upper pouch is composed. It often seems to consist of nothing more than mucous membrane with no muscle fibres present for perhaps 0.5 cm. or more, and in these cases we do not see how it is possible to make more than one layer of sutures, as many authors advise when doing the anastomosis. We feel that, even when good tissue is available, a second layer is inviting devascularization of either or both ends, with its attendant risk of fistula.

We use four basic everting mattress sutures which are named north, east, south, and west by the surgeon as he puts them in and hands the ends, which are clamped with a distinctive pattern of forceps, to the assistant. When these are in place the two ends of the oesophagus can usually be approximated if a gentle continuous pull is sustained on them by the assistant while the surgeon "kneads" the ends together, often over a period of minutes.

Usually, one single suture is then placed between each mattress suture, making a total of eight sutures around the periphery, and the parietal pleura is approximated over the anastomosis. Careful closure of this layer is most important.

At this stage the anaesthetist withdraws the rubber catheter over which the anastomosis has been performed and replaces it by a length of fine polythene tubing which is passed across the anastomosis under direct palpation and vision. This tube is for feeding and is passed just through the cardia.

The chest is then closed in the usual way with fine chromic catgut after two intercostal drainage tubes have

been inserted, one up to the site of the anastomosis and the other ending at the apex of the pleural cavity.

Neostigmine is usually given, estimated on the initial dose of tubarine used, 1 ml. of tubarine containing 2.5 mg. The amount of neostigmine required is estimated by the formula:

$$\frac{2.5 \times \text{initial dose of tubarine}}{20}$$

If thoracotomy reveals that for one reason or another direct end-to-end anastomosis is impossible, the fistula, if present, is closed and a gastrostomy and cervical oesophagostomy performed.

Definitive correction of the defect can then be made subsequently by staged operations, and it would seem that in the present state of knowledge the use of a segment of transverse colon is more likely to be successful than oesophago-gastrostomy or oesophago-jejunostomy.

The use of a skin-lined antethoracic oesophagus with its many stages and liability to stricture would seem to have no place in the treatment these days.

Use of Gastrostomy

Apart from those cases where primary anastomosis cannot be performed, the use of gastrostomy must obviously be assessed on its merits in each case. Some surgeons (Leven *et al.*, 1952; Gross, 1953; Clatworthy, 1955; Roberts *et al.*, 1955) advise its routine use either at the time of, or shortly after, every primary anastomosis, but we feel that the polythene tube inserted as described at the conclusion of the anastomosis is quite adequate for nutritional requirements.

If, however, a stricture should occur at the anastomosis, retrograde bouginage with Tucker bougies by means of a string through a gastrostomy is a very useful and effective method, and we have used this in four cases in this series. We find that cineradiography of the oesophagus with the image intensifier is a marked improvement on conventional methods and a valuable aid in assessing changes in the degree of stricture.

We always use two strings, as breakage of the loops of the Tucker bougies is not uncommon, and if this should occur the spare one can be employed to pull through another before any further dilatation is done. The replacing of a single broken string is somewhat tedious and involves the use of a very fine filiform bougie introduced through the stricture from above under direct vision, a suckling bronchoscope being passed down the oesophagus. We use the type of bougie described by Hubbard and Leven (1950). The bougie is passed into the previously washed-out stomach and the end picked up by sinus forceps, the jaws of which are observed by means of a cystoscope introduced alongside the forceps. The string is then tied on to the end of the catheter and pulled back.

Retrograde insertion of a ureteric catheter, via the cystoscope, into the oesophagus is theoretically simpler, but in practice the cardiac opening is most difficult to visualize in an infant.

Post-operative Care

While the subject-matter of this report is primarily concerned with the surgical aspects of the condition, it would be wrong to assume that these are the most important. The contribution of the surgeon, while very necessary, is nevertheless only a fraction of the work involved. It is no understatement to say that, post-operatively, the fate of these children rests almost entirely on the work of the paediatrician and the nursing staff, all of whom spend many worried days and restless nights looking after these very ill patients.

Most of the previously mentioned authors have covered this aspect of post-operative care very fully, and there is little to add to the accepted routines. It is essential that during the first week or two the child has a special nurse right around the clock. She turns him hourly, sucks out his pharynx at the slightest suspicion of mucus, and keeps an accurate report of changes in the colour, pulse, and respiration. Constant observation of the drainage bottles to ensure that the tubes are patent and not blocked by blood clot is essential. After removal of the tubes a careful watch for evidence of a pneumothorax is of vital importance.

Daily *x*-ray films are taken for the first two or three days, and antibiotics are used routinely, usually chlortetracycline, 10 mg. per lb. (22 mg. per kg.) body weight per day.

Neonates are notoriously poikilothermic, and care must be taken not to overheat them during the operation and during the first few days.

A direct-vision laryngoscope, a good suction apparatus, and a few sucker ends must be beside the cot throughout every 24 hours of the first two weeks or so.

The apical drainage tube is usually removed at 24 to 48 hours if the lung is expanded, and the other is left *in situ*, still connected to the water seal bottle, until about the fifth or sixth day.

Feeding

Feeding is begun post-operatively with glucose-water hourly, and two-hourly after the first 24 hours. Feeds are given through the polythene tube, and after 48 hours half-strength expressed breast milk is given, being changed to full strength on the fourth day. These feeds are also given via the polythene tube, which is removed about the ninth day in uncomplicated cases. Chlortetracycline is given by the same route, the intravenous drip being taken down as soon as the operation is over. The volume of the feed is gradually increased and the intervals are lengthened. Two of our patients, discharged on the ninth and tenth post-operative days respectively, were by that time having normal breast-feeds. We believe it important to begin normal oral feeding to stimulate swallowing as soon as possible. Even though supplementary feeds may have to be given via a gastrostomy tube, a certain amount of oral feeding is desirable.

TABLE II.—*Birth Weights*

Survivors		Non-Survivors*	
lb. oz.	g.	lb. oz.	g.
7 12	3,515	5 12	2,608
7 2	3,222	5 15	2,693
7 8	3,402	3 8	1,588
7 4	3,289	4 12	2,155
6 4	2,835	4 14	2,211
5 8	2,495	6 14	3,118
5 13	2,637	6 3	2,807
6 14	3,118	5 1	2,296
Average: 6 12	3,062	5 5	2,495

*One patient was not weighed.

Results in Present Series

Weight and Mortality.—It is generally agreed that, other things being equal, the higher the birth weight, the lower the mortality, and this is certainly borne out in this series. The best case was home on breast-feeding on the ninth post-operative day. The average period in hospital of the others was three to four weeks. Of our 17 cases, 14 had a primary anastomosis, one was diagnosed only at necropsy, one was never fit for operation, and one in Group 2a had a gastrostomy only; both of these latter died. Of the 14 patients with primary anastomoses, nine survived and five died, giving a survival rate of 64%.

Late Results.—Four of the survivors had some degree of stricture post-operatively. These all had a gastrostomy and were treated by dilatation with Tucker bougies as described previously. Of these cases one is now swallowing quite normally and the gastrostomy is closed, two are still receiving retrograde bouginage at increasing intervals, and one after three years has a persistent stricture for which operative repair has been undertaken. The stricture has been excised and the trimmed ends of the oesophagus have been anastomosed satisfactorily. An interesting point in

this case is that the walls of the oesophagus were tissue-paper thin, and at the original operation seemed to consist of mucous membrane only, whereas well-formed and apparently normal oesophagus had developed in the three-year interval before excision of the stricture. The mass of scar tissue at the stricture was incredibly hard, forming a block about 2.5 by 2 by 2 cm., and it was not surprising that it did not respond to frequent dilatation.

Summary and Conclusions

The experience of one team with 17 cases of atresia of the oesophagus is described.

Special points in surgical technique and care of these babies are stressed. Results in relation to the findings are given.

It is felt that the knowledge of the simple diagnostic procedures, the possibilities of operative repair, and the location of the nearest unit willing to undertake these cases should be widely disseminated among general practitioners and midwives.

Experience with these cases is invaluable, from the medical and nursing points of view, in reducing the mortality and morbidity rates. Therefore cases should if possible be sent to an experienced team, and the extra journey with the baby is far outweighed by the advantages of getting the case to such a unit.

Great care in performing the anastomosis pays handsome dividends and speed is of no importance.

Special nursing round the clock is essential for these babies in the first few post-operative days.

We thank Mr. Kent Harrison for allowing us to include two of his Cambridge cases in this series. We are grateful to Dr. Douglas Gairdner and his paediatric team and the anaesthetists at Addenbrooke's Hospital for their encouragement and help, without which these patients would not have survived. We thank Miss Sylvia Treadgold for the drawings.

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An "emergency" identification card for the protection of patients on long-term anticoagulant therapy is now available to physicians from the American Heart Association and its affiliates. The card was developed as a result of requests from physicians seeking to protect their patients on anticoagulants in case of accident, dental surgery, or other treatment that may induce bleeding. In case of emergency the card advises that a doctor be called, since the patient may require an antidote. The card contains space for the name, address, and telephone number of the patient's physician, the type of anticoagulant prescribed, and the patient's blood group. Samples of the card are obtainable from the American Heart Association, 44, East 23rd Street, New York City.

PRIMARY ATYPICAL PNEUMONIA AND HIGH SEDIMENTATION RATES

BY

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The diagnosis of atypical pneumonia originated at the time when, following the introduction of antipneumococcal sera and sulphonamides, a group of cases of pneumonia was distinguished from the majority by a failure to respond to these forms of therapy (Finland and Dingle, 1942). Since then further microbiological, serological, and radiological investigations have resulted in the recognition of several subdivisions of this group which are aetiologically, if not clinically, distinguishable. These include the aspiration pneumonias and the pneumonias associated with rickettsial Q fever, ornithosis, the acute specific fevers, and infections by the influenza viruses and the adenoviruses.

The serum of many of the cases of atypical pneumonia which remain unaccounted for contains antibodies which agglutinate homologous red cells in the cold (4° C.). The constitutional upset in these latter cases is often greater, and the radiological changes are often more extensive, than would be expected from the pulmonary symptoms and signs, which are often slight. The white blood count is normal, or only slightly increased, in the early stages of the illness, and the serum may contain agglutinins against the streptococcus M.G. The dramatic response to penicillin therapy usually seen in pneumonia does not occur, but, in some epidemics at least, treatment with one of the tetracycline antibiotics has been found to be effective. The condition has been transmitted by bacteria-free filtrates of respiratory tract secretions to volunteers, and from them to a second series of experimental subjects (Commission on Acute Respiratory Diseases, 1946), but no virus has yet been generally agreed to be responsible. It is for this condition that many now reserve the description of primary atypical pneumonia.

Raised titres of cold agglutinins are sometimes found in other respiratory diseases such as influenza, ornithosis, and pneumococcal pneumonia. These conditions are unlikely to be misdiagnosed as primary atypical pneumonia if titres of cold agglutinins of 1 in 128 or more are required before the diagnosis of the latter is accepted, and even more unlikely if a fourfold increase in titre is observed in serial specimens. Many of these other pulmonary disorders can also be excluded by further serological or bacteriological tests.

Observations

As part of the routine investigation of nine sporadic cases of primary atypical pneumonia, in which the clinical diagnosis, based on the features described above, was confirmed by the demonstration of significant titres of cold agglutinins, estimations of the erythrocyte sedimentation rate (E.S.R.) were made by the method of Westergren (1921). Readings were made of the fall of the red cells in a 200-mm. tube after one hour. Seven of the nine patients had an E.S.R. of over 90 mm. when first estimated, and the E.S.R. of another of these patients was over 80 mm. on admission, rising later to 98 mm. (Cases 1–9, Table I). Four of the nine

TABLE I.—*Sedimentation Rates and Cold Agglutinin Titres in 16 Cases of Primary Atypical Pneumonia*

Case No.	Age and Sex	E.S.R. (in italics) in mm. in First Hour (Westergren) and Cold Agglutinin Titre — Weeks of Illness						
		1	2	3	4	5	6	7
1	52 F		*117* 1/512	1/16,384	*30* 1/128			
2	27 F		*91* 1/512		*16* 1/32			
3	25 F	*83*	*85* 1/512	*98*	*80* 1/64			
4	33 F		*120* 1/128	*12* 1/256				
5	64 F			*126* 1/4,096		*75* 1/4,096		*58* 1/32
6	36 F				*91*		*62* 1/128	*106* 1/32
7	34 F		*138* 1/1,024	*40* 1/1,024	*7* 1/256			
8	58 M		*10*	*40* 1/640	1/250	*40* 1/320	*33* 1/160	(8th week) *25* 1/64
9	78 M		*105* 1/80		*95* 1/128	*122* 1/8		
10	61 F	*126* 1/1,280		*92* 1/640	*97* 1/160	*92* 1/320		
11	78 M		*160* 1/16		*90* 1/128	1/64		
12	67 M		*102* 1/512	*63*	*49* 1/256	*31* 1/128		
13	72 M	*115* 1/64			*80* 1/128	*60* 1/128	*43* 1/32	
14	60 M	*98* 1/256		1/128	*79* 1/32		*59* 1/64	*61* 1/32
15	65 M			*54* 1/1,024	1/1,024	*5* 1/256		
16	81 M		*101* 1/128	*93*	*104* 1/64	*120* 1/64		

patients showed readings of 120 mm. or more. A further patient (Case 10) with hypertensive heart disease, who was admitted with a recurrence of left ventricular failure apparently precipitated by a respiratory infection, had an E.S.R. of 126 mm., which prompted the examination of the serum for cold agglutinins. These were present in a titre of 1 in 1,280.

Such high sedimentation rates are not found with great frequency in acute pneumonia in present-day hospital practice. Retrospective examination of the notes of 160 patients with acute pneumonia uncomplicated by non-cardiorespiratory disorders (group II), showed that 22 (14%) had an E.S.R. of over 90 mm. at the time of admission (Fig. 1). A rate of over 120 mm. in one hour was exceedingly rare. Four of these 22 patients were thought on clinical grounds to have a virus pneumonia.

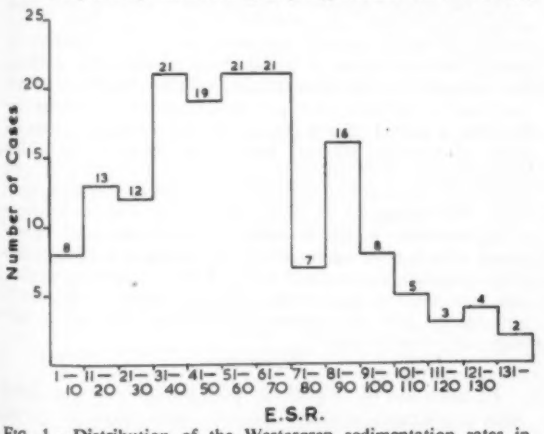

FIG. 1.—Distribution of the Westergren sedimentation rates in mm. in the first hour of 160 patients with acute pneumonia (Group II).

A further 77 consecutive patients with acute pneumonia (group III) had estimations of the E.S.R. and of the cold agglutinin titre made soon after admission to hospital. The cold agglutinin titre was measured by a method similar to that described by Dacie (1956). Any patient with an E.S.R. of over 80 mm. or whose serum contained cold agglutinins was re-examined on one or more occasions. Six patients (8%) showed significantly raised and varying titres of cold agglutinins (Cases 11–16, Table I), and five of these had an E.S.R. of over 90 mm. (Fig. 2). These patients with high

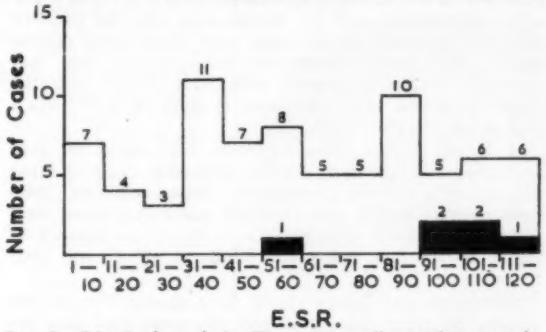

FIG. 2.—Distribution of the Westergren sedimentation rates in mm. in the first hour of 77 patients with acute pneumonia (group III). Shading shows cases with high cold agglutinin titres.

cold agglutinin titres were often not clinically distinguishable from the other cases of pneumonia in this third group, and are not therefore completely comparable to the sporadic cases of atypical pneumonia (Cases 1–9). Over one-third of the cases in groups II and III with very high sedimentation rates but without raised cold agglutinin titres had some complicating condition, such as pleural effusion or bronchiectasis, which might have explained the finding of higher rates than are usually seen in pneumonia.

Discussion

It must be admitted that many writers in the years 1930–9, including Motzfeldt (1932) and Douglas-Wilson (1939), often found Westergren sedimentation rates above 90 mm. in cases of lobar pneumonia during the first week of illness. This frequency of high sedimentation rates is at variance with present experience. Douglas-Wilson (1939) found, however, that such high levels were not reached until the third day of the illness, at which stage nowadays antibiotic therapy usually will have controlled the infection. Two other possible reasons for the discrepancy are that diagnostic criteria have broadened and that the type of case admitted to hospital has changed.

In some of our cases of atypical pneumonia minor symptoms had been present for many days before the condition had become serious enough to lead to their admission to hospital for treatment. This gradual onset, and therefore the later stage in the illness at which the E.S.R. was first estimated, might be one of the factors responsible for higher rates being found in this group, but it would not explain why such very high levels were found in almost every case.

The high sedimentation rates found in our cases are not due to excessive aggregation of red cells consequent upon the action of the cold agglutinins present, for the following reasons: (1) The association was not invariable. (2) The levels of the E.S.R. did not appear to be directly or constantly related to the titres of cold agglutinins; thus Case 4 showed a fall in the E.S.R. from 120 mm. to 12 mm., while the cold agglutinin titres rose from 1 in 128 to 1 in 256, and Cases 5 and 7 showed no change in their titres of cold agglutinins while their E.S.R. fell by more than 50 mm. (3) Estimations of the sedimentation rate at different temperatures show that the rate remains high even if the test

is carried out at 37° C., at which temperature the agglutinins are inactive, and that the rate bears no consistent relationship to the temperature (Table II). (4) Cold agglutinins are

TABLE II.—*Westergren E.S.R. at Different Temperatures*

Case No.	E.S.R. in mm. in First Hour at Temp. of:		
	4° C.	Room Temp.	37° C.
3		98	70
7		138	163
9		105	125
10	12	92	80
13	80	80	103
16	55	93	82

adsorbed on to the red cells when separation of plasma and cells is carried out at 4° C. In one case, after the patient's red cells, separated in this way, were mixed with normal plasma, a normal Westergren sedimentation rate was obtained, but when normal cells were mixed with the patient's plasma, after separation at either 4 or 37° C., a high E.S.R. was obtained.

It is not denied, however, that high titres of cold agglutinins can sometimes be the immediate cause of rapid sedimentation at room temperature. Jessen and Bing (1940) have reported such a case in which active agglutinins were present in sufficient concentration at 19° C. to produce an E.S.R. of 106 mm., while the E.S.R. at 40° C. was only 55 mm.

Hardwicke and Squire (1952) have shown that, in the absence of gross changes in red cell shape and size, the E.S.R. depends principally upon alterations in one or more of the plasma fractions: fibrinogen, α_2-globulin and γ-globulin. A significant elevation of the plasma fibrinogen was found in all nine of our cases in which this was estimated, and in most cases there was an increase in serum globulin and a slight decrease in serum albumin (Table III).

TABLE III.—*Blood Proteins in Cases of Primary Atypical Pneumonia*

Case No.	Serum Proteins in g./100 ml.			Plasma Fibrinogen in g./100 ml. (Normal: 0·2–0·4)
	Total	Albumin	Globulin	
3	6·7	4·9	1·8	0·56
5	6·7	4·2	2·5	
7	6·3	3·4	2·9	
9	7·0	2·1	4·9	0·74
10				0·52
11	7·1	3·2	3·9	0·76
12	5·1	2·3	2·8	0·6
13	6·1	2·6	3·5	1·03
14	7·4	3·3	4·1	0·82
15	6·2	2·6	3·6	0·63
16	6·8	3·4	3·4	0·69

Electrophoretic examination of the serum of each of Cases 8 to 16 showed an increase in globulins, particularly in the γ and less obviously in the α_2 fractions. Some cases of pneumonia with very high sedimentation rates but without raised cold agglutinin titres showed similar plasma protein abnormalities, except that an increase in α_2-globulin was seen more frequently. As Cases 8 and 15, in which very high E.S.R.s were not detected, also showed plasma protein changes apparently similar to those of the other cases of atypical pneumonia, the way in which these changes produce the high sedimentation rate must be a subtle one. The situation does not appear to be comparable to that in another virus infection, lymphogranuloma venereum. In this condition the very rapid rates sometimes found are related to the high concentration of γ-globulin which occurs (Waldenström *et al.*, 1951).

MacLean and Parnell (1955) have described a case of pneumonia associated with a high titre of cold agglutinins and with a haemolytic anaemia; a similar case has been reported by Stewart and Friedlander (1957). The Westergren sedimentation rates were 158 and 156 mm. in one hour respectively. The pneumonia in one of our patients (Case 7) was also complicated by haemolytic anaemia; her E.S.R. was 138 mm. at room temperature and 163 mm. at 37° C. The extremely high figures in these three patients are possible because of the reduction in the packed cell volumes, but the mechanism of the rapid sedimentation would otherwise appear to be the same as in the rest of our cases. Shaw and Fry (1955) reported that the highest sedimentation rate found in 66 cases of acute infections of the chest was 113 mm. in one hour in a case of virus pneumonia with raised cold agglutinin titre; a personal communication confirms that the Westergren method was employed. The great majority of references in the literature to sedimentation rates in atypical pneumonia with high cold agglutinin titres relate, however, to estimations by the Wintrobe or similar methods. The rates recorded were normal or only moderately increased.

Simultaneous estimations of the sedimentation rate by both the Westergren and Wintrobe methods were carried out in each of six of our more recently observed patients (Table IV). The disparity in the results of the two methods

TABLE IV.—*Westergren and Wintrobe Sedimentation Rates of Same Blood Samples*

Case No.	Sedimentation Rate in mm. in First Hour	
	Westergren	Wintrobe
9 i	105	13
9 ii	95	7
10	92	36
11 i	100	54
11 ii	90	14
13 i	115	43
13 ii	80	40
14	79	55
16 i	101	43
16 ii	93	31

is obvious, in particular two patients (Cases 9 and 11) had normal Wintrobe rates when the Westergren rates were over 90 mm. in one hour.

The occurrence of similarly anomalous results of sedimentation rate estimations, an increased rate by the Westergren method being accompanied by a normal or only slightly increased Wintrobe rate, has been reported by Gilmour and Sykes (1951), Goldberg *et al.* (1952), Goldberg and Conway (1952), and Alexander (1953). The Westergren method in each case provided a better index of the clinical state of the patient. Factors which appear to play a part in producing the discrepancy include the chemical properties of the anticoagulant used (Goldberg *et al.*, 1952), the method of filling the Wintrobe tube (Alexander, 1953), and dilution of the blood (Lewi, 1954). The height of the column is especially important when very high sedimentation rates are being looked for; using the Wintrobe method, it is impossible with non-anaemic blood to obtain a fall of more than about 55 mm. owing to the packing of the red cells in the shorter (100-mm.) tube.

The association which we believe exists between very high sedimentation rates and primary atypical pneumonia is not related to one particular epidemic, but to the disease in general, because Cases 1–10 occurred sporadically, without obvious epidemiological connexion with one another. They were seen in two hospitals in London and one in Southampton over a period of five years. We do not suggest that all cases of primary atypical pneumonia show a very high sedimentation rate, nor that every case of pneumonia with such an E.S.R. will be found to have a raised cold agglutinin titre. The finding of an E.S.R. of over 90 mm. in one hour in all but three of the 16 cases of pneumonia with significantly raised cold agglutinin titres reported here is, however, remarkable enough to justify further statistical studies, and meanwhile to lead to this diagnosis being considered in any patient with an unusual pneumonia who has a very high sedimentation rate.

Summary

Thirteen out of 16 patients with pneumonia associated with significantly raised titres of cold agglutinins in the serum had Westergren sedimentation rates of over 90 mm. in one hour when first examined.

Nine of these patients were sporadic but consecutive cases of clinically atypical pneumonia, of whom seven had an E.S.R. of over 90 mm. on admission and four had rates of 120 mm. or more at some stage of their illness. These levels are much higher than those commonly seen in acute pneumonia.

The high sedimentation rates are not due to the excessive aggregation of red cells produced by the cold agglutinins. The plasma protein abnormalities which occur do not appear to be unusual or specific to this form of pneumonia.

Such very high rates can be demonstrated only by the Westergren method; the Wintrobe method may give disproportionately low or even normal results.

If a patient with acute uncomplicated pneumonia has an E.S.R. of over 90 mm. the diagnosis of primary atypical pneumonia should be considered, especially if there are any other unusual features.

We are most grateful to Dr. Neville Oswald for his advice and to the physicians of St. Bartholomew's, the Royal Free, the Royal South Hants, and St. Thomas's Hospitals for their permission to include details of patients who had been under their care.

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PRIMARY ARACHNOID CYSTS

REPORT OF TWO CASES

BY

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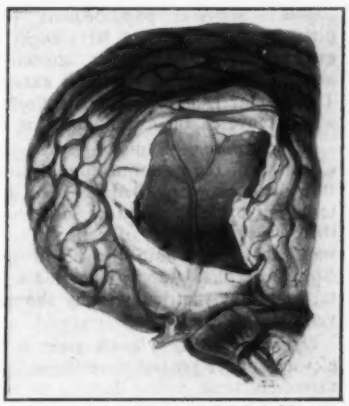
Richard Bright (1831) gave a short account of cysts arising in relation to the surface of the brain, and there is little doubt that some of them were cysts of the arachnoid, as the accompanying reproduction of his original illustration shows. A long time elapsed before any further noteworthy contributions to this subject were made.

de Martel and Guillaume (1930) reported seven cases of arachnoid cysts in the posterior fossa and stressed the sudden onset of headache with neck stiffness, suggesting the diagnosis of meningitis or subarachnoid haemorrhage. Mullin (1932) described two cases in which a cyst in the cerebellopontine angle produced a syndrome resembling that of an acoustic neurinoma: arachnoid cysts are commonly found associated with acoustic tumours, but in Mullin's cases the internal auditory meatus was clearly exposed and a tumour excluded. The membrane was not examined microscopically; therefore it is possible that the cysts were ependymal in origin as in a case described by Hardman and Jefferson (1938).

Characteristics

Tönnis, at the meeting of the Society of British Neurological Surgeons in Berlin in June, 1937 (unpublished), described his experience of eight cases of "congenital cysts of the cisterns" simulating intracranial tumours. This was a most valuable contribution in which the characteristics of arachnoid cysts were defined as follows: The membranes correspond to the meninges in their structure; signs of inflammation in the cyst wall are absent; the cystic fluid is clear and usually xanthochromic, and coagulates spontaneously after removal.

McConnell and Douglas (1939), writing on intracranial cysts, included examples of what they termed "subarachnoid cysts." Their illustrations make it clear that the outer wall of the cysts was composed of arachnoid, and the inner wall of pia mater. Three examples were cited: in the first the cyst occupied most of the right anterior fossa, in the second the anterior half of the right temporal fossa, and in the third the midline of the posterior fossa. In all three instances it appeared as though the underlying brain was deficient. Macroscopically the arachnoid and pia forming the cyst walls were normal. The fluid of the cysts was not analysed and there was no microscopical examination of the membranes.



Reproduction of Richard Bright's illustration of an arachnoid cyst in the left Sylvian fissure. (Kindly lent by Mr. James Hardman.)

Horrax (1924) reported some cases of Cushing's of midline cysts of the posterior fossa causing increased intracranial pressure. The cysts, however, appeared to be dilatations of the cisterna magna, and they were attributed to inflammatory adhesion of the membranes, though evidence of inflammation was lacking in most of the cases; examples of cysts in the cerebellopontine angle associated with otitis media were also encountered. Cases similar to Cushing's were described by Allen and Corkill (1937); in two of them the cysts were apparently separate from the cisterna magna and were therefore true arachnoid cysts. These authors also favoured the inflammation theory, though no histological or other evidence was given to support it.

Successful removal of a circumscribed cyst of the leptomeninges involving the spinal cord and cauda equina was reported by Spiller, Musser, and Martin (1903). The walls of the cyst were described as transparent, but again no histological examination was carried out; in a subsequent paper, however, Spiller (1909) attributed such lesions to inflammation, and hence the origin of the term "circumscribed serous spinal meningitis." Spiller was supported in his belief by Horsley (1909), who reported his cases under the title of "chronic spinal meningitis"; he suggested that in some instances syphilis or gonorrhoea was the responsible infection.

Stookey (1927) believed there was no justification for the view that arachnoid cysts are of inflammatory origin, though he reported his own case under the title of "Adhesive Spinal Arachnoiditis."

Scrutiny of case records in the literature lends abundant support to Stookey's opinion, but histological reports on the membranes are rarely given. Therefore it seems worth

while to record the following cases in which detailed description of the cysts and histological reports are available.

Case 1

A man aged 21 was admitted to hospital on May 16, 1941, complaining of headache, vomiting, and diplopia. Ten weeks previously he had received a severe blow on the chest while playing football. Two weeks later he began to have headaches, mostly frontal, but sometimes occipital; the frontal headaches extended behind the eyes. He felt sick in the morning and sometimes vomited. For four weeks diplopia had occurred on looking to the right. There was nothing relevant in the past and family histories.

On examination the following abnormal signs were found: bilateral papilloedema (one dioptre); dilated pupils, right more than left; slight weakness of the right external rectus; left upper neurone facial weakness; and absence of abdominal reflexes except the right lower one. The plantar responses were unaffected. Nothing abnormal was discovered on examination of the other systems.

Investigations.—Radiography of the skull showed decalcification of the posterior clinoid processes. Lumbar puncture done elsewhere had revealed a pressure of 300 mm.; tests for protein, chlorides, and sugar were normal, and there was no excess of cells. The Wassermann reaction was negative in both the blood and cerebrospinal fluid. Electroencephalography suggested a lesion in the *left* parietal lobe, but ventriculography showed displacement of the ventricles to the *left*.

Operation (May 17).—A right fronto-temporal flap was elevated under general anaesthesia. As the dura mater was extremely tense it was decided to tap the anterior horn of the right ventricle, but a small incision in the dura revealed a bluish-looking membrane beneath it. A subdural haematoma was suspected, but a brain cannula passed through the membrane showed yellow fluid. A sample was sent for examination. A further quantity of fluid was withdrawn to slacken the dura, which was then opened. The Sylvian fissure was widely separated by a large cyst extending well forward into the anterior fossa and downward into the middle fossa. When the cyst was opened the island of Reil was clearly visible, with many tortuous branches of the middle cerebral artery running across its surface. The outer or superficial wall of the cyst was formed by a *uniformly transparent* membrane which appeared to be continuous with the arachnoid around the periphery of the cavity, where it was fused with the inner wall formed by macroscopically normal pia mater and underlying brain. A small entirely separate loculus at the anterior end of the middle fossa was separated from the rest of the cyst by a very thin membrane. There were no adhesions between the cyst and the dura mater. The superficial wall of the cyst was removed and preserved for histological examination; the deep wall, being composed of pia mater, was left undisturbed. There was no tendency at all for the brain to expand and fill the space left by the removal of the cyst; the appearance was as though part of the cerebrum was missing.

The patient made a rapid recovery. By July 14 he was free from symptoms, and the papilloedema and other physical signs had disappeared, except that the left abdominal reflexes were not so brisk as those on the right. Air encephalography, performed through the cisternal route eight weeks after operation, showed the ventricles to be normal in shape and position, but they were about twice the size observed before removal of the cyst. A large amount of air had collected in the space previously occupied by the cyst.

Examination of cyst fluid on May 17 showed slightly blood-stained amber fluid with a total protein of 460 mg. per 100 ml. (considerable excess of globulin, Pandy plus 4, Nonne–Apelt plus 3). There were 13 white cells and 22,664 red cells per c.mm.

Histology of Cyst Wall (Professor Dorothy Russell).—"The wall of the cyst is composed of arachnoid membrane thickened by fibrosis, and showing (*a*) considerable recent focal haemorrhage, and (*b*) areas of greatly increased vascularity associated with chronic inflammatory infiltration and considerable numbers of macrophages containing iron pigment. A piece of dura mater overlying the cyst showed no abnormality. The appearances are consistent with a traumatic origin, but traumatic changes in a previously existing arachnoid cyst cannot be excluded."

Case 2

A boy aged 10½ months was admitted to hospital on May 16, 1947, because of enlargement of the head and vomiting. Labour had been difficult, lasting 51 hours. The head was observed to be larger than normal at birth, but was not measured. There had been four bouts of vomiting over the period of five months before admission. There was no history of meningitis or head injury.

On examination the maximum circumference of the head was found to be 23½ in. (59.6 cm.) (normal for the age, 17–18 in. (43–45.5 cm.)), the fontanelles were large and tense, and the cranial sutures were widely separated. The limited neurological examination possible at this age was negative.

On May 20 ventriculography was performed with needles passed through the lateral angles of the anterior fontanelle. Only 40 ml. of C.S.F. was replaced with air; the lateral ventricles were shown to be very dilated but not displaced. Though the third ventricle was not visualized it was decided to proceed immediately with exploration of the posterior fossa. 4 ml. of 0.4% indigo carmine was injected into the ventricles so that the patency or otherwise of the aqueduct could be determined at operation.

Operation (May 20).—Under infiltration anaesthesia, a midline muscle-separating posterior fossa exposure was carried out. When the bone was removed a bluish-looking membrane could be seen through the thin dura mater on the right side. A small incision was made in the dura and the cyst tapped. Clear colourless fluid was withdrawn; *there was no trace of indigo carmine in this fluid.* The dura mater was then reflected and the cyst was opened; there were no adhesions between the dura and the cyst. Unfortunately the fluid escaped too quickly for any to be sent for analysis. Pressure on the anterior fontanelle did not cause any further fluid to flow from the cyst, but instead it caused ballooning of the cisterna magna, which, by aspiration through a hypodermic needle, was shown to contain dye. *Thus the cyst was proved to be separate from the cisterna magna.* The outer wall of the cyst appeared to be fused around its periphery with the pia mater covering the cerebellum; and the latter was displaced upward and to the left.

When seen four years after the operation the patient was speaking normally but was only just beginning to walk unaided. The maximum circumference of his head was then 23 in. (58.4 cm.), a fraction of an inch less than at the time of operation.

Histology (Dr. E. A. Atkinson).—The tissue received had the appearance of normal arachnoid membrane; there was no evidence of inflammation.

Discussion

These two records demonstrate clearly the strict criteria of primary arachnoid cysts; the outer walls were formed by arachnoid membrane, as confirmed by histological examination, and the inner walls by the pia mater of the underlying brain surface. In Case 1 it was possible to collect the fluid; it was xanthochromic and contained a level of protein well above that of the cerebrospinal fluid; in Case 2 there was also proof of the nature of the membranes, and though the fluid was not analysed it was conclusively demonstrated by the dye technique, and by pressure on the

anterior fontanelle, that the cyst was not a distended cisterna magna and that it did not communicate with the subarachnoid space beyond its boundaries.

There was no evidence in the histories, at operation, or on histological examination, of a bacterial meningitis or neoplastic process. There was no history of direct head injury in either instance, but in Case 1 there had been a blow on the chest a few weeks before the onset of symptoms. It is well recognized that compression injuries of the thorax sometimes cause secondary damage to the brain (Rowbotham, 1945). It appears likely that the changes in the arachnoid reported by Professor Dorothy Russell in this instance were of traumatic origin, as she suggests, and that the symptoms were thus precipitated by the injury; but it is inconceivable that the large cyst, insinuating its way deeply in the Sylvian fissure, could have arisen solely from the effects of a recent injury; in support of this assertion is the fact that air encephalography carried out eight weeks after operation showed persistence of the space formerly occupied by the cyst—an unlikely finding if the brain had been merely displaced by a traumatic cyst.

Conclusion

The cause of the majority of arachnoid cysts is unknown; the term "primary arachnoid cysts" is suggested for this group and "secondary arachnoid cysts" for those which can be attributed to injury or inflammation, and for those which are associated with tumours.

It may be that primary cysts result from an error of development of the leptomeninges and the underlying nervous tissue.

In the cases reported by McConnell and Douglas (1939) and in my first case the cysts appeared to occupy an irregular space, giving the impression of absence rather than displacement of nervous tissue, and there was no tendency for the cavity to disappear after removal of the cyst; in Case 1 the space was demonstrated by air encephalography eight weeks after operation—unlikely if the brain had been simply displaced. It seems impossible to escape the conclusion that the cyst in this case was congenital.

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The third annual volume of the *Bibliography of Medical Reviews* is to be published in June. Review articles listed in volumes 1 and 2 were gathered as a by-product of the *Current List of Medical Literature*, in which they also appeared, but in a different form. With volume 3, however, the collection of review articles is extended to cover all the journals currently received by the National Library of Medicine, Washington. The result is that volume 3 includes references to 600 reviews not in the *Current List* as well as to the 2,300 articles that are. The references are arranged by subject and there is a separate author index; the 2,900 review articles listed cover clinical and experimental medicine and allied fields and most of them were published in 1957. Copies of volume 3 will be available from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C., at an estimated price of about $1.25.

SYMPTOMS AND CLINICAL ASPECTS OF DIABETES MELLITUS

BY

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The division of cases of diabetes mellitus into relatively well-defined groups has simplified the clinical picture and led to greater success in the management of the disease. The response to insulin was the basis of Himsworth's (1939) classification. In general, the young and thin patient tended to be insulin-sensitive; the elderly and obese patients with hypertension tended to be insulin-resistant. Further, the onset of the disease in the sensitive diabetic was generally sudden and severe, and ketosis rapidly developed if insulin was withheld. In the insensitive group the onset was usually insidious and ketosis was rarely present.

Plasma insulin estimations confirmed clinical observations that all diabetic children, most adults under 40, and many over 70 are insulin-deficient (Bornstein and Lawrence, 1951a, and 1951b). In the insulin-resistant group plasma insulin levels are near normal, and Lawrence (1951, 1954) employed the terms "lipoatrophic" and "lipoplethoric" diabetes to describe the two opposite examples encountered. Lipoatrophic diabetes is so rare that it can well be regarded as "a collector's piece." In contrast, the lipoplethoric type accounts for the majority of obese middle-aged diabetics, being twice as common in women as in men.

The essential purpose of the present investigation is to determine the incidence of symptoms in the ketosed and non-ketosed groups of diabetic patients. A study is also made of the way each case presented, the clinical picture, and the response to treatment.

Method and Material

The paper is based on the case histories of 300 patients attending the diabetic clinic at the Royal Devon and Exeter

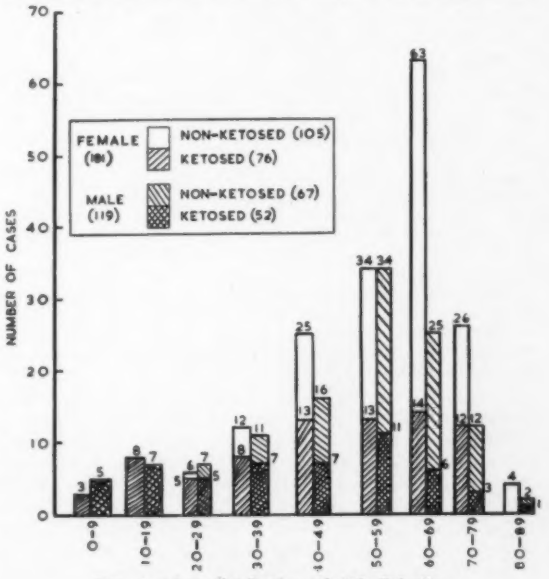

FIG. 1.—Age distribution of 300 diabetics.

Hospital. The only condition of selection was that the initial diagnosis had been made after 1951.

Information was obtained by personal interview, and by study of case records. A questionary was also completed by each patient, and supplementary questions were framed to find out if any of the symptoms remained after satisfactory stabilization. Any such symptoms were ignored unless they could be accounted for by a recognized diabetic complication.

The 300 cases of diabetes mellitus comprised 181 females and 119 males, a ratio of 1.5 to 1. The age distribution by decades at the time of onset of diabetic symptoms is shown in Fig. 1. It will be seen that the peak age of onset in women was in the seventh decade, and in men in the sixth decade. There were almost equal numbers of females and males below the age of 40. The ages ranged from 3 years to 85 years.

The incidence of ketosis is based on the clinical test for ketonuria devised by Smart and Darling (1948). Ketonuria was present in 128 (43%) cases (76 females and 52 males). The relationship between ketonuria and age groups is shown in Fig. 1.

Diagnosis

In 240 (80%) patients the diagnosis was made by the family doctor. Severe diabetic ketosis or coma was present in 25 new cases; and in only 5, which presented as acute abdominal emergencies, was the condition not recognized before admission to hospital.

In 12 (4%) cases symptomless glycosuria of diabetic origin was an incidental finding at a routine medical examination or when seen for an unrelated condition.

The remaining 48 (16%) cases were first diagnosed in hospital. These patients attended with diabetic symptoms or complications although their nature had not been previously recognized. For example, eight women presented with pruritus vulvae or mycotic vulvovaginitis, and five with toxaemia of pregnancy, a stillbirth or large baby, or a history of habitual abortions.

Mode of Onset

Sudden onset of symptoms, occurring within a 24-hour period, was recorded in five patients (Cases 1–4 and 10). In each patient, previously in good health, severe ketosis rapidly developed. None of these patients was obese, and in only one was there a diabetic heredity.

Case 1.—A schoolboy aged 14 complained of thirst, frequency, and excessive appetite on returning home from a four-mile walk one January afternoon. The following morning he was admitted to hospital with severe diabetic ketosis (blood sugar 414 mg./100 ml.).

Case 2.—A farm-worker of 24 became very thirsty one spring afternoon. During the next day his tongue became dry and sore, and frequency and blurring of vision occurred. On the third day glycosuria and ketonuria were discovered (blood sugar 460 mg./100 ml.).

Case 3.—A Service man aged 30 played rugby and went to bed without taking part in any celebrations. He awoke with extreme thirst and had to pass urine three times before rising. These symptoms persisted and were associated with tiredness, anorexia, and dimness of vision. Within two weeks he was in a diabetic coma.

Case 4.—A housewife aged 63 spent one afternoon in August sitting in the sun by the sea. On the way home she was sick in the bus, and on arrival complained of severe headache, thirst, and frequency. Within 48 hours she was in coma (blood sugar 612 mg./100 ml.).

In 12 (4%) cases the onset was rapid, occurring within a six-day period, and on diagnosis ketonuria was present in 10 patients. In 30% a gradual onset was recorded, symptoms occurring within a period of from six days to two months. In 66% the mode of onset was indefinite and not definable within a two-months period.

The acute form of onset within a two-months period occurred in 75% of patients under 40 years and in 54% of the ketosed group. An indefinite onset was reported in 75% of the patients over 40 and in 78% of the non-ketosed group. Clearly, an acute onset was common among young diabetics with ketosis, whereas an insidious onset was common among older patients without ketosis.

Classical Symptoms

A lowered incidence of classical symptoms of disease can be expected only if early diagnosis is achieved. The recognition of minimal symptoms and signs, with adequate treatment, will prevent the clinical picture from developing fully.

The accepted classical symptoms of diabetes mellitus are polyuria, polydypsia, polyphagia, loss of strength, and loss of flesh. One or other of these symptoms could be elicited in 95% of diabetic patients, yet as a group they occurred in less than 19%. All five classical symptoms were present in 24% of patients with ketosis, compared with 15% of those without ketosis. They occurred as a group over twice as often in patients under 40 years (37%) as in those over 40 (15%).

Polyuria.—The validity of polyuria as a cardinal symptom of diabetes has been challenged by Barach (1941). Defining polyuria as a urinary output of greater than 2.5 litres during a 24-hour period, he found this occurred in only 18% of his patients, although 75% of them complained of frequency of micturition (pollakiuria). Although he suspected that "the physician of yesterday took the patient's word for the existence of polyuria," many accounts of this symptom have appeared in the literature. In this survey, frequency of micturition during the day or at night was the presenting symptom in 15% of diabetic patients. It occurred in 81% of patients, being present in 87% of those with ketosis and 75% of those without ketosis. In the ketosed group this symptom, in common with thirst, usually responded to insulin therapy within a few hours. In the obese group strict dietetic measures produced the same result within a few days. Nocturnal enuresis was noted in three children, and in one man this was the presenting symptom. Podolsky (1937) included backache as one of the characteristic symptoms of diabetes, and considered this was due to distension of the renal capsules by the quantity of urine. In this series there were only two cases in which lumbar pain could not be attributed to pyelonephritis or renal calculi.

Polydypsia.—Thirst occurred in 88% of patients (91% of the ketosed group and 81% of the non-ketosed group), being the presenting symptom in 48%. The tongue, mouth, and lips were dry, and often painful, in 21% of cases. These symptoms were almost three times as common in the ketosed group (33%) as in the non-ketosed group (12%), and may herald the onset of diabetic coma. In two instances hoarseness and dysphagia accompanied severe thirst. The mouth usually tasted foul, but occasionaly a sweet taste was noted. Obstinate constipation has been described as a visceral manifestation of diabetic neuropathy, though in general it is due to dehydration. It is so common a cause of complaint in otherwise healthy people that, unless its duration closely corresponded to that of thirst and frequency of micturition, this symptom was not regarded as due to diabetes. Recorded in this way, constipation was present in 29% of cases, comprising 37% of the ketosed group and 24% of the non-ketosed group, and was a presenting symptom in 1% of patients. Nocturnal diarrhoea occurred in 1% of cases.

Polyphagia.—In this survey unnatural appetite was much the least common of the classical symptoms, being noticed by 24% of patients (29% of the ketosed group and 20% of the non-ketosed group), and being the presenting symptom in only 2%. In spite of this excessive appetite, over 80% of patients had lost weight. A truly voracious appetite was encountered in a bricklayer, aged 27, who resorted to stealing in order to buy enough food to satisfy his need. In a few patients there was a craving for sugar.

Loss of Strength.—Lassitude occurred in 74% of diabetics, being observed in 81% of the ketosed group and 69% of the non-ketosed group. It was the presenting symptom in 16% of the cases.

Loss of Flesh.—Loss of weight of more than 10 lb. (4.5 kg.) occurred in 68% of cases and was the presenting symptom in 14%. It was observed that 22% of patients had lost between 21 and 40 lb. (9.5 and 18 kg.) as against 38% in Barach's series. Furthermore, only 8% lost over 40 lb. (18 kg.) compared with 24% of Barach's cases. In this survey, loss of weight was recorded in 75% of cases with ketosis and 63% of cases without ketosis. Further study of these patients showed that only 20% of the ketosed group compared with 60% of the non-ketosed group were obese before the onset of diabetic symptoms. This finding is in accordance with the accepted view that loss of weight without previous obesity is a characteristic feature of the diabetic patient with ketosis.

Additional Symptoms

Pruritus.—Pruritus vulvae did not occur in any patient under 15 years of age. It was observed in 62% of those over 16, occurring in 54% of the ketosed group and 68% of the non-ketosed group, and was the presenting symptom in 27% of cases. Although pruritus is said to be particularly common in obese middle-aged diabetics, in this series the incidence was almost exactly the same in each decade. In 10% of patients generalized pruritus also occurred. Localized genital pruritus was recorded in 11% of men and was the predominant complaint in 4%. In a further 18% of cases generalized pruritus was also present.

Visual Disturbances.—45% of patients complained of impairment of vision before diagnosis, and this was recorded in 49% of the ketosed group and 42% of the non-ketosed group. It was a presenting symptom in 6%. Visual impairment was not confined to the elderly diabetic, occurring in 41% of patients below 40—the youngest affected in this way being a girl of only 4 years—in 46% of cases between 40 and 60, and in 47% over 60. Diplopia occurred in three patients, an ocular palsy being demonstrable in the following case:

Case 5.—A housewife aged 62, with no diabetic symptoms, presented with a two-weeks history of double vision and frontal headache. Apart from a right third nerve palsy, no other abnormal physical signs were detected. Glycosuria was noted: the fasting blood sugar was 272 mg./100 ml. Within two months of diabetic control with insulin the ocular nerve palsy had completely disappeared.

Retrobulbar neuritis is a recognized, though rare, complication of diabetes.

Case 6.—A ship's fireman aged 44, with no diabetic symptoms, was first seen by Dr. J. D. Spillane, at Cardiff Royal Infirmary, with a five-months history of gradual failure of vision. For two months he had complained of frontal headache, and over a seven-day period his vision had so deteriorated that he was unable to read newspaper headlines. He was a non-smoker, only on rare occasions had he taken alcohol, and had received no drugs. On examination the visual acuity was 2/36 in each eye. Marked pallor of both optic disks was present. Studies of the visual fields revealed bilateral central scotomata. No other abnormal neurological signs were detected. The fasting blood sugar was 220 mg./100 ml., and ketonuria was present. Radiographs of the skull and chest, electroencephalogram, and cerebrospinal fluid were all normal. The Wassermann reaction of the blood and C.S.F. was negative and the Lange curve normal. Air encephalography and a right carotid angiogram were normal. Within four weeks of starting insulin no scotoma was found in the left eye, and the scotoma in the right eye had decreased in size. Vision in the left eye (6/24) showed considerable improvement, though it had deteriorated in the right eye (2/60). His visual acuity over a four-year period has fluctuated. The left eye improved to 6/9, the right eye remaining constant at 6/60. The appearances of the fundi are unchanged, and no additional neurological signs have developed. The insulin requirements have progressively increased.

Paraesthesiae.—A sensation of numbness, tingling, or pins-and-needles was reported by 32% of cases (34% of the ketosed group and 31% of the non-ketosed group), but was the presenting symptom in only one patient. Subjective sensory disturbances occurred in 24% of patients under 40, in 35% between 40 and 60, and in 34% over 60. Paraesthesiae occurred generally in both hands and feet, but occasionally were limited to only one digit, to one hand or foot, or to one limb. In two cases girdle paraesthesiae were present, and in another the lower abdominal wall and both legs were also affected. One patient complained of severe numbness in both legs and a feeling as of walking on a pad before the diagnosis of diabetes was made.

Peripheral Pain.—It is known that conditions producing peripheral pain include diabetic neuropathy, peripheral vascular disease, and salt and water depletion, so considerable variation in the quality, duration, and intensity of pain is only to be expected. 42% of cases complained of peripheral pains. They comprised 43% of those with ketosis and 41% of those without. It was the presenting symptom in 1% of cases. Of these patients, the pain was localized to the legs in 91%, the arms were also affected in 6%, and girdle pain was reported in 3%. Cramp in the calf muscles, particularly at night, was frequently noted, and in two cases a history of lightning pains was given. In almost one-third of patients paraesthesiae were also reported. Pain was a symptom in 37% of diabetics under 40, the youngest one being a girl 9 years old. It occurred in 39% of patients between 40 and 60, and in 45% of those over 60. Clearly, as the age distribution is approximately constant, it would seem that peripheral vascular disease cannot be regarded as an important aetiological factor.

Loss of Appetite.—This was a symptom in 18% of all diabetic patients. It occurred in 29% of those with ketosis and 10% of those without ketosis. It was the presenting symptom in only one case. The sudden change from an excessive appetite to anorexia was of considerable diagnostic significance, being an almost constant manifestation of impending severe ketosis or diabetic coma.

Abdominal Pain and Vomiting.—A history of abdominal pain, nausea, and vomiting, either alone or in combination, was obtained in 18% of cases—33% of the ketosed group and only 7% of the non-ketosed group. In five patients with severe diabetic ketosis the pain was so intense and sudden in onset that the provisional diagnosis of an acute surgical emergency had been made. Their ages ranged from 15 to 78 years. In each case the abdominal pain and vomiting rapidly subsided after correction of the dehydration and diabetic ketosis. Nevertheless, although diabetic pre-coma may mimic an acute abdominal emergency, it is always possible that both conditions may in fact be present.

Case 7.—A female clerk of 22, with mild diabetic symptoms of three months' duration, presented with a four-day history of acute abdominal pain and vomiting. On admission she was drowsy, her breath smelt strongly of acetone, and air-hunger, dehydration, and signs of peripheral vascular failure were present. There was no abdominal tenderness or rigidity. The blood sugar was 850 mg./100 ml. Her condition responded initially to intensive therapy with insulin and intravenous fluids, but within 10 days a recurrence of severe abdominal pain, vomiting, and ketosis coincided with the onset of jaundice due to gall-stones.

Sexual Disorders.—Loss of libido or impotence occurred in three men under 40, and amenorrhoea in five women between the ages of 17 and 38. In all but three patients ketonuria was present, and insulin therapy was followed by complete recovery.

Personality Changes.—Watson (1838) reported that in some diabetic cases "the once vigorous mind becomes feeble, oblivious and vacillating—the once amiable temper, fretful, suspicious and intolerant." Personality changes occurred in 5% of patients before diagnosis, being the presenting symptom in two cases. Apart from the first decade, no age group was exempt, and of the 15 cases affected (9 females and 6 males) 10 had ketonuria. In one young married man acute depression, irritability, forgetfulness, and impotence were present for five weeks. Although previously temperate, he now sought escape from his troubles in frequent bouts of drunkenness.

Miscellaneous Findings.—Classical diabetic symptoms closely followed the onset of angina of effort in two cases. Electrocardiograms showed no evidence of myocardial ischaemia, and after satisfactory diabetic control had been attained no recurrence of effort pain was reported during the

next three years. In one man myocardial infarction precipitated a mild, though undiagnosed, case of diabetes into severe ketosis. Partial loss of hair was reported by a young boy and by two women over 60. Together with loss of toenails, this was the presenting symptom in one adult case. White spots on the shoes, or soiling of clothes or bed-linen, was the presenting symptom in one of eight persons affected. One young man noticed that his perspiration gave a "sweet apple-like smell." Swelling of the ankles was observed by two men under 30 and in one over 50. In one case the pitting oedema completely subsided after satisfactory stabilization but returned with the reappearance of ketosis. Puffiness around the eyes was noticed by one woman under 30. There was no evidence of diabetic nephropathy in any of these four cases. Two young adults experienced delay in healing of the gums following tooth extraction. Pre-existing acromegaly and basophilism were each noted in one case, thyrotoxicosis in two cases, and a non-toxic goitre in eight. One man presented with gout; his mother and maternal grandparents had gout, but there was no diabetic heredity.

Symptom-complex of Hypoglycaemia

A prodromal stage of diabetes resembling mild insulin shock has been described by Allen (1953). In the following two cases the prodromal symptoms were identical to those later experienced with an insulin reaction.

Case 8.—A labourer of 33 gave an eight-years history of episodes of hunger, profuse sweating, dizziness, headache, trembling of the limbs, tingling of the lips and tongue, and mistiness of vision. During a six-weeks period he developed lassitude, thirst and frequency, excessive appetite, and a dry, sore tongue. The fasting blood sugar was 342 mg./100 ml., and ketonuria was present.

Case 9.—A schoolmaster of 41 suddenly became dizzy and faint and developed a profuse cold sweat while sawing wood just before his tea was due. The following morning a similar episode occurred while pumping up his bicycle tyres before breakfast, and again while cycling home to lunch. These symptoms subsided after he had eaten. During the next few days he developed a craving for sugar. Two weeks later glycosuria was discovered. Fasting blood sugar was 75 mg./100 ml. The glucose-tolerance curve was normal, but the renal threshold was low, being below 124 mg./100 ml. He reported again six months later with a week's history of thirst, frequency, tiredness, and misty vision. Ketonuria was present and blood sugar three hours after food was now 410 mg./100 ml.

Emotional Glycosuria

Barach (1950) has quoted the popular saying, "in Wall Street when stocks go down, sugar goes up." Almost 25% of patients in this series attributed their diabetic state to overwork, or domestic or financial problems which had occurred within a year of the presenting symptoms. Williamson (1918) reported similar findings in 40% of his cases. Although one sympathizes with the young schoolboy who considered that the stress of end-of-term examinations caused his diabetes, careful analysis of patients' statements failed to produce any evidence that anxiety was of aetiological significance. The following case may be a possible exception.

Case 10.—A shop assistant aged 19, with no diabetic heredity and of previously good health, noticed excessive thirst within a few hours of hearing that her fiancé had been killed. During the next day she also complained of frequency. When admitted to hospital two months later her fasting blood sugar was 410 mg./100 ml., and severe ketosis was present.

Hypertension

Using the grading of Wood (1952), hypertension was found in 147 of 241 (61%) cases over 40, being mild in 61.4% of cases, moderate in 32%, and severe in 6.6%. The only significant difference between a control group and the diabetic group was observed in women between 50 and 70. Masters, Marks, and Dack (1943) reported hypertension in 53.4% of non-diabetic women in the sixth decade and in 67.7% in the seventh decade. In the diabetic women of this survey, hypertension was recorded in 76.5% and 77.8% of these age groups respectively. Hypertension was present in 79 of 115 (68.7%) obese diabetics and 68 of 126 (54%) non-obese diabetics over 40. Further, 51 of 147 (34.7%) diabetic cases with hypertension were more than 20% above standard weight; this degree of obesity was shown in only 18 out of 94 (19.1%) cases with normal blood pressures.

Heredity

All surveys based on questioning are open to criticism, as the existence of diabetes in relatives may be unknown. In this investigation the incidence of heredity was 34.3% (Table I).

TABLE I.—*Incidence of Heredity in Relation to Age Groups in 300 Diabetic Cases*

	Under 40 (59 Cases)	40–69 (197 Cases)	Over 70 (44 Cases)	Total (300 Cases)
Both hereditary and familial	3 (5·1%)	8 (4·1%)	—	11 (3·7%)
Hereditary	18 (30·5%)	34 (17·3%)	3 (6·8%)	55 (18·3%)
Familial	4 (6·8%)	22 (11·1%)	11 (25%)	37 (12·3%)
Total	25 (42·4%)	64 (32·5%)	14 (31·8%)	103 (34·3%)

Obesity

The incidence of obesity varies considerably in different surveys, being subject to individual interpretation due to lack of precise definition. In this investigation only people who are 10% or more above standard weight are considered obese.*

Obesity was present in 127 of 283 (44.9%) diabetics over 16 before they noticed the first symptoms, and was recorded in 37.3% of the males and 49.7% of the females. In the 40–69 age group obesity was present in 52.3% of cases—46.7% of men and 55.7% of women.

Ketonuria was discovered in 25% of obese diabetics compared with 50% of those who were not obese. The incidence of ketosis and non-ketosis based on age, sex, and weight is given in Fig. 2. It is evident that before the onset of diabetic symptoms there is a greater tendency for marked obesity to be present in women than in men (Fig. 3). In fact, there were 17 women who were more than 40% above standard weight but only one man; four women were over 80% above standard weight.

Weight reduction is essential in the treatment of obese diabetic patients. If this is effectively achieved, the glucose-tolerance curve may return to normal. Relaxation of dietetic control may be followed by a return of symptoms.

Case 11.—A housewife of 47 attended with a six-months history of lassitude, thirst, and frequency. Her normal weight was 42% above standard. Her symptoms disappeared on a weight-reducing diet alone, and her fasting blood-sugar levels fell from 250 to 112 mg./100 ml. When the carbohydrate intake was increased from 100 to 140 g. a day her hyperglycaemia and symptoms returned.

Of the obese diabetics, 42% were controlled by diet alone compared with 21% of the non-obese. In the age group 40–69 years, 46% of the total obese cases, and 54% of those more than 20% above standard weight required no insulin. Whereas 37.5% of the obese cases below 50 years were controlled by diet, not one of the non-obese cases in the same age group could be treated effectively without insulin.

A hereditary or family history was obtained from 35.4% of the obese group and 32.7% of the non-obese. The following case illustrates the relationship between diabetes, obesity, and heredity.

Case 12.—A housewife aged 43 weighed 21 st. (133 kg.). Her only sister (19 st.—120 kg.) and her father (22 st.—140 kg.) also had diabetes. Her mother, who weighed 9 st. (57 kg.), was not a diabetic. Her paternal grandmother and this grandmother's father were said to be diabetics and over 20 st. (127 kg.) in weight.

*Calculated for age, sex, and height (Association of Life Insurance Directors and Actuaries of America, New York 1, 1912).

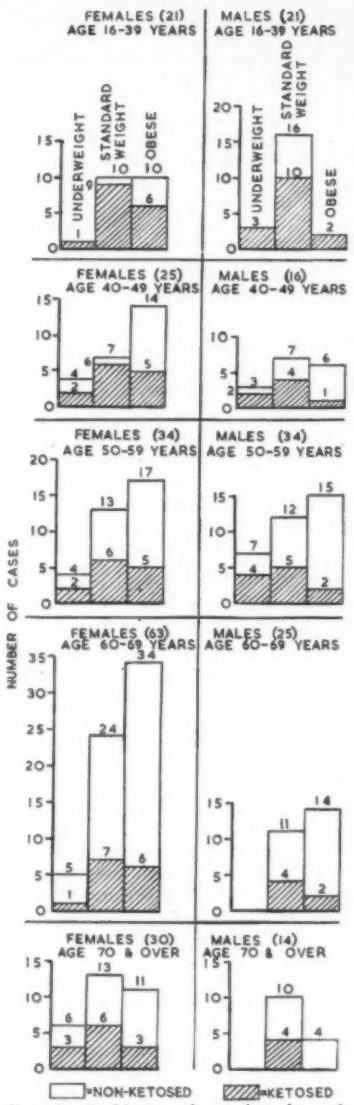

FIG. 2.—Incidence of non-ketosis and ketosis in groups based on sex, age, and weight.

Underweight

Out of 283 cases, 33—12% of males and females over 16—were 10% or more below standard weight before the onset of diabetic symptoms. The underweight cases comprise 16% of the ketosed group and 9% of the non-ketosed group. There was a total of 92 (32.5%) cases underweight on diagnosis, this being found in 45% of those with ketosis and 24% of those without ketosis. The weight of two patients before the occurrence of symptoms, and the weight of a further nine patients on diagnosis, was more than 30% below standard (Table II). The fact that diabetes is evidently very rare in people who are normally 30% or more below standard weight may be of diagnostic value when symptomless glycosuria is discovered.

Case 13.—A single woman aged 59 was seen with symptomless glycosuria. Her normal weight was 32% below standard. A postprandial blood-sugar level was 212 mg./100 ml. A glucose-tolerance test gave a normal fasting blood sugar of 100 mg./100 ml. and a "lag curve."

In order to control the disease insulin was required in every patient under 60, and in almost two-thirds of those over 60, who were underweight on diagnosis.

TABLE II.—*Incidence of Underweight in 283 Diabetic Patients Over 16 Years of Age*

Per cent. Below Standard Weight	No. of Cases Underweight	
	Before Onset of Diabetic Symptoms	At Time of Diagnosis of Diabetes
10–19%	26	57
20–29%	5	24
30–39%	2	7
Over 40%	—	4
Total cases underweight	33 (12% of diabetics)	92 (32·5% of diabetics)

Trauma

Transient glycosuria, not constituting true diabetes, is an occasional sequel of trauma. However, injuries, particularly fractures, may be followed by the onset or exacerbation of symptoms in a potential or previously well-controlled diabetic patient. In part, this may be due to the period of enforced inactivity which necessitates regulation of the diet and insulin dosage. An additional factor may be excessive production of the diabetogenic hormone as a reaction to stress.

Case 14.—A housewife aged 53, with no diabetic heredity or symptoms, was admitted to hospital with a fractured tibia. During the next few days she complained of thirst, frequency, and deterioration of vision. Her fasting blood sugar was 274 mg./100 ml. and ketonuria was present.

Infection

A history of infection within three months of diagnosis was obtained from 85 of 300 (28%) patients. It was recorded in 33% of those with ketosis and 25% of those without ketosis. Five patients admitted to hospital in diabetic coma had an upper respiratory or pulmonary infection during the previous week. An infective process was the presenting symptom in 9% of all diabetic patients. Ulceration or gangrene of the toes or feet was not entirely confined to elderly diabetics, and was the presenting symptom in each of the nine cases so affected.

Staphylococcal infection above all others may provoke glycosuria and hyperglycaemia, even in hitherto apparently healthy people, and may precipitate manifest diabetes in a person so predisposed (Himsworth, 1949). In 36 of 88 (42%) cases the infection was staphylococcal in origin, comprising furunculosis (23), carbuncles (5), infection of urinary tract or pyelonephritis (4), ischio-rectal abscess (3), and lobar pneumonia (1).

Case 15.—A market gardener of 65, with no diabetic heredity, presented with a 10-day history of thirst and frequency following the appearance of a carbuncle. His fasting blood sugar was 240 mg./100 ml., and ketonuria was present. Insulin was required for 14 days. As his weight was 25% above standard he was advised to continue with a reducing diet. Glycosuria and ketonuria reappeared some six months later, when he developed a septicaemia due to *Staphylococcus pyogenes*; fasting blood sugar was 230 mg./100 ml. After a further nine months he complained of dysuria, and culture of the urine revealed a profuse growth of *Staph. pyogenes*. Since then fasting blood-sugar levels over a two-year period have been normal.

Mumps was followed by diabetic symptoms in three boys aged 7, 11, and 14, and in one woman aged 62, by 1, 6, 12, and 19 months respectively. With the exception of Case 16, these findings may be incidental, although no such close relationship existed in other specific fevers.

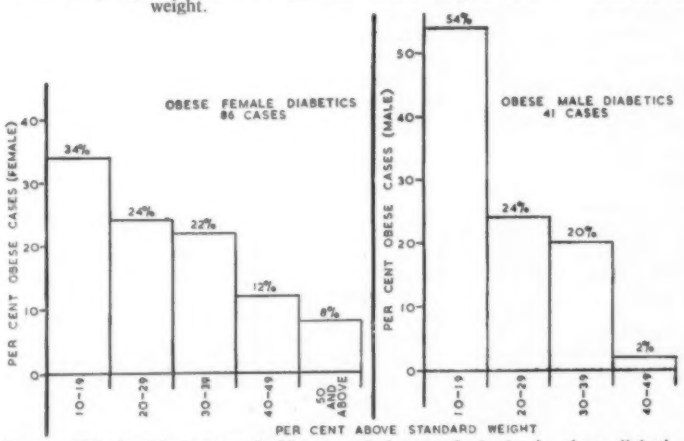

FIG. 3.—Relationship between incidence and degree of obesity in obese diabetic patients.

Case 16.—A boy aged 7, with no diabetic heredity, developed generalized abdominal pain during the first few days of mumps. His expected recovery was delayed, and within four weeks he complained of tiredness, thirst, frequency, and a sore, dry tongue. In less than two months he was admitted to hospital with diabetic ketosis.

Thomas Shapter, physician to the Exeter Dispensary, reported that every one of 83 diabetic patients observed between 1825 and 1834 had "terminated in tubercular consumption." In the present survey, undertaken in Exeter little more than a century later, only 2 out of 300 diabetic patients developed signs of active pulmonary tuberculosis.

Conclusions and Summary

A study was made of 300 cases of diabetes mellitus. In 80% of patients the diagnosis was made by the family doctor; in 16% it was made in hospital when advice was sought for symptoms or complications of unrecognized diabetes; and in 4% symptomless glycosuria of diabetic origin was discovered at routine medical examination.

At the time of diagnosis ketonuria was present in every patient under 20 years, in approximately two-thirds of patients in the 20–39 age group, and in one-third of patients of 40 and over. It was present in 25% of patients over 16 years of age who were obese and in 50% who were not obese. An acute onset of symptoms, occurring within a two-months period, was common among diabetics under 40 with ketonuria, while an insidious onset was common among older patients without ketonuria.

A comparison was made of the symptoms of the disease in the ketosed and non-ketosed groups of cases. One or other of the five classical symptoms of diabetes was present in 95% of cases. As a group they were present in only 24% of patients with ketonuria and in 15% of patients without ketonuria.

Loss of weight without previous obesity was a characteristic feature of the ketosed group. A sudden change from an excessive appetite to anorexia was also of considerable diagnostic significance. Loss of appetite often preceded the onset of acute abdominal pain, nausea, and vomiting in cases of severe diabetic ketosis. Pruritus vulvae was the only diabetic symptom which occurred more often in the non-ketosed group. Visual disturbances, paraesthesiae, and peripheral pain did not vary significantly with age.

The incidence of heredity was 34.3%. Before the onset of symptoms 45% of patients over 16 years were 10% or more above standard weight; 43% were of standard weight, and 12% were 10% or more below standard weight. The incidence of marked obesity in diabetic patients over 40 was almost twice as great in the presence of hypertension. In only two cases was the normal weight more than 30% below standard.

In order to control the disease, insulin was required in 94% of the ketosed group and in 55% of the non-ketosed group. Every patient under 60 years who was underweight on diagnosis required insulin, while 42% of obese diabetics could be controlled by diet alone.

I wish to thank the consultant staff of the Royal Devon and Exeter Hospital for permission to publish details of their cases. I am also grateful to Dr. D. E. Olliff for advice in the preparation of this paper.

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LITTRE'S HERNIA

BY

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"L'apendice de l'Ileon (quit formoit la Hernie) etoit un canal membraneux de figure conique." Thus, in 1700, Alexis Littre in his *Observation sur une nouvelle espece de hernie*, described the diverticulum that is involved in the hernia which to-day bears his name (Littre, 1719).

Despite his recognition of the existence of this diverticulum, it was not until 1809 that Johann Friedrich Meckel elucidated its anatomy and embryology. He pointed out that the diverticulum persisted through failure of the vitelline duct to obliterate, a process which normally occurs during the seventh week of embryonic life.

Complications of Meckel's Diverticulum

The incidence of the diverticulum is variously given as between 0.1 and 3% (Strohl and McArthur, 1939). It may be situated on the terminal ileum as far proximally as 66 in. (167.5 cm.) from the ileo-caecal valve (Jay *et al.*, 1950). Complications due to its presence, though not very common, are often lethal in their consequences. The chief among these are inflammation; haemorrhage, or perforation if it contains ectopic gastric mucosa; intestinal obstruction due to volvulus and bands; tumours; and strangulation within a hernial sac.

Cullen (1954) recorded an unusual case of an acutely inflamed diverticulum which had herniated through the foramen of Winslow into the lesser sac. Doolin (1929) reports one of his experiences when a Meckel's diverticulum was found in the hernial sac at a routine inguinal herniorrhaphy, and returned to the abdomen; six days later he was obliged to reoperate and remove the diverticulum from the apex of an intussusception which it had initiated.

It is on account of the complications that all authors are unanimous in recommending removal of every diverticulum found at laparotomy; and, in view of its variable position, at least the terminal 5 to 6 ft. (150 to 180 cm.) of ileum—not 2 ft. (60 cm.), which is so often quoted—must be displayed to exclude its presence.

Definition of Littre's Hernia

In his paper Littre discussed the post-mortem findings in two cases in which "an appendix of the ileum" had become incarcerated in inguinal herniae. He defined this "new hernia," and made the following relevant clinical observations concerning the pre-operative diagnosis: "(i) The patient goes to stool throughout the whole course of the illness, as the intestinal canal is uninterrupted. (ii) There is no vomiting, or by comparison, less frequently than with other herniae—it is never faeculent. (iii) The belly is never fat, stretched or full with wind, as in ordinary herniae. (iv) The tumour (in the groin) is formed more slowly, and never becomes so large. (v) Inflammation, fever, pain or other symptoms which may accompany this peculiar kind of hernia, are less severe and take longer to manifest themselves than in other herniae."

He goes on to describe the morbid anatomy: "(1) In ordinary cases of hernia the entire circumference of the intestinal body is engaged in the hernial sac. In this hernia there is only part in the sac. (2) In ordinary herniae the intestine is doubled like an arc; in this hernia the portion of the intestine is simple, is situated perpendicularly, and terminated by a very distinct end. (3) An ordinary hernia is often formed by intestine and omentum together. This particular kind is always made by the intestine alone."

From his description it is clear that a *true* Littre's hernia is one containing a Meckel's diverticulum alone; should ileum or other abdominal viscera be included it is a *mixed* Littre's hernia. Furthermore, it is implied, though not specifically stated, that the diverticulum is incarcerated or strangulated in the sac—a point emphasized by Fishback (1944) and Davis (1954).

Incidence of Littre's Hernia

In a series of 680 cases of strangulated femoral hernia Frankau (1931) noted only one case involving a Meckel's diverticulum; in 654 strangulated inguinal herniae he reports that 4 Littre's herniae were found. (The respective figures for Richter's herniae in these two groups were 77 and 15.) Conversely, in 600 cases of (pathological and non-pathological) Meckel's diverticulum, Forgue and Riche (1907) found 52 (8.7%) within hernia sacs. In a further three papers on Meckel's diverticulum (Collins, 1950; Jay *et al.*, 1950; Brookes, 1954), covering a total of 196 cases, not a single case of Littre's hernia is recorded. In 18 cases of complicated Meckel's diverticulum, Hashemian and Murray, (1954) did not find one Littre's hernia.

That the diverticulum, the only occupant of a hernial sac, should become strangulated is a rare occurrence. The exact number of cases described is difficult to ascertain with any degree of accuracy, "the designation strangulation and incarceration being not always in keeping with the description of operative findings" (Weinstein, 1938).

The following is the report of one such case.

Case Report

A married woman aged 82 was admitted to the Leicester Royal Infirmary on January 21, 1957, complaining that she had had a (discharging) lump in the left groin for the preceding week. Her practitioner had diagnosed an inguinal adenitis "although no primary source of infection could be found." She was treated with oxytetracycline, and the condition improved until two days before admission, when it "suddenly flared up again, suppurated, and leaked through the left labium majus." At no time had she suffered any severe pain; there was no vomiting, and her bowel habit was undisturbed. She had no other symptoms.

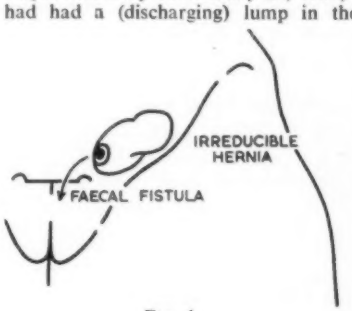

FIG. 1

In 1940 she had been admitted to the Leicester General Hospital with bronchitis and a reducible left femoral hernia. Eight days after admission, however, the hernia became tense and painful and she vomited twice. The same evening femoral herniotomy was carried out. The sac was found to contain omentum and a small loop of "strangulated but not gangrenous bowel," which was replaced. She made an uneventful recovery and was discharged one month after admission. Over the past 13 years or so she has had easily reducible bilateral inguinal herniae—at the time of admission only the right was reducible.

Examination showed her to be a rather emaciated, frail old lady, in full possession of all her faculties and in no obvious pain. Her pulse was 80, B.P. 160/90, and temperature 98° F. (36.7° C.). She had emphysema of both lungs, but no cardiac abnormality. The abdomen was soft without distension. No visible peristalsis was observed. In the left groin there was a large "inguinal abscess" the size of an orange—it was irregularly lobulated, and was covered by reddened slightly tender skin. At its medial extremity, which pointed at the labium majus, light-yellow feculent material was discharging through a break in the skin. There was well-marked subcutaneous crepitation (Fig. 1). The previous femoral herniotomy scar was not visible. In the right groin there was a large easily reducible indirect inguinal hernia. A pre-operative diagnosis of strangulated Richter's hernia with spontaneous faecal fistula was made.

Operation

Under general anaesthesia, a transverse muscle split incision was made above the inguinal mechanism. Extraperitoneal dissection exposed the neck of an inguinal hernial sac. At this point the peritoneum was opened and the sac explored. From the antimesenteric border of a loop of terminal ileum a Meckel's diverticulum protruded into the sac. It was fairly easily reduced and was found to be 2 in. (5 cm.) in length. At approximately ½–¾ in (1.3–2 cm.) from its base it had been strangulated, and at this point the wall had sloughed and was in free communication with the sac. The fundus of the diverticulum was completely necrotic and was filled with feculent material (Fig. 2).

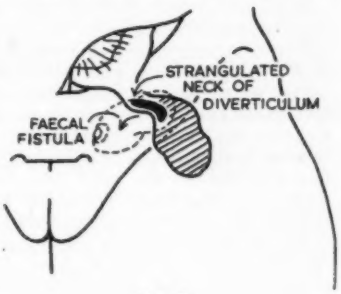

FIG. 2

The anomalous pouch was amputated through healthy tissue near its base, and the resulting defect in the ileum was repaired transversely with two layers of running chromic catgut.

In view of the gross contamination the hernial sac was left undisturbed but excluded from the general peritoneal cavity by dissection of healthy peritoneum from around its neck, so that the peritoneal defect could be closed with a running suture. Through a stab incision, a corrugated rubber drain was led extraperitoneally down to the site of peritoneal closure (also the "internal os" of the hernial sac), and the abdominal wound was closed in layers. The faecal fistula was enlarged by an incision from the exterior; the faecal material was aspirated, and the resulting cavity was flushed with hydrogen peroxide. A second corrugated rubber drain was inserted into this cavity (the "external os" of the hernial sac).

Penicillin and streptomycin were given parenterally after operation and the drains were shortened as the discharge diminished.

The patient was finally discharged from convalescent home 32 days after admission, fully recovered. The surgical wound had healed by primary intention and the fistula wound was then quite dry.

When seen two months later the patient had fully recovered and there was no recurrence of the hernia.

Recorded Cases of Littre's Hernia

From a review of the literature (Ekehorn, 1901; Bunts, 1904; Pabst, 1910; Lanman, 1924; Littler, 1924; Sweet, 1930; Gray, 1934; Weinstein, 1938; Rodnaev, 1939; Dé Felice, 1949; Kazmann and Barnett, 1950; Giordano, 1953; Davis, 1954; Payson *et al.*, 1956) it will be seen that: (1) Strangulation of a Meckel's diverticulum is more common in femoral than in inguinal herniae. 44 cases of the former and 17 of the latter are recorded. (2) The ages of the patients varied from 3½ weeks to 82 years. (3) The sex

incidence in femoral herniae was 11 males, 25 females, and 8 not stated or not ascertained; and in inguinal herniae it was 10 males, 3 females, and 4 not stated or not ascertained. (4) Perforation of the diverticulum into the hernial sac occurred in four cases, and through the skin (as a faecal fistula) in six cases of femoral hernia; of the six who developed faecal fistula, five survived (83%); of the four who had perforation into the sac none survived. The corresponding figures for inguinal hernia were two perforations into the sac and one through the skin—all three survived.

In addition to inguinal and femoral Littre's herniae, cases have been recorded of Meckel's diverticula in umbilical (Bianchi, 1927), sciatic (Brodnax, 1924), and lumbar (Rodnaev, 1939) herniae.

Discussion

Numerous cases of Meckel's diverticula lying *free* in hernial sacs have been described, these being more common in inguinal than in femoral herniae. This is attributed to the fact that the intestinal coils found in a hernia are those possessing the longest mesentery. Anatomically the longest mesentery is possessed by the lower ileum, which is also the site of Meckel's diverticulum when present (Bunts, 1904).

In addition, a host of *mixed* Littre's herniae are on record. The strangulation of a Meckel's diverticulum (itself not a particularly common occurrence) as the sole content of a hernial sac (true Littre's hernia) is decidedly uncommon.

The prognosis in strangulated Littre's hernia is more favourable than in a strangulated mixed Littre's or even, for that matter, the strangulation of a bubonocele or femoral hernia; for whereas in the former the faecal stream is unimpeded, in the latter two types there is complete obstruction, and death is inevitable unless the obstruction is relieved by operation, spontaneous reduction of the hernia, or by the formation of an external fistula (Friedman, 1931). In the case of true Littre's hernia, despite the uninterrupted passage of bowel content, perforation of the strangulated bowel does occur, probably in those cases in which feculent material, entrapped distal to the point of strangulation, leads to distension and necrosis of the blind diverticulum.

In the reported cases perforation occurred in 10 femoral herniae and 3 inguinal herniae. In the former, only those patients who developed a spontaneous faecal fistula survived (five out of six); all four of those who had perforations into the sac, without the safety-valve mechanism of a faecal fistula, died. In the three cases of perforated Littre's inguinal hernia (two into the sac; one externally as a fistula) there was no mortality.

In the case described above the patient had minimal systemic effects, and was sent into hospital with a provisional diagnosis of an indolent inguinal abscess, this being very similar to the case described by Weinstein (1938). After further appraisal in hospital a strangulated Richter's hernia was diagnosed; this is the common pre-operative misdiagnosis. That this old lady survived the mishap which befell the congenital anomaly that she had borne for 82 years must, I think, be attributed to the fact that she developed a spontaneous faecal fistula, which saved her from peritonitis and toxic absorption.

Summary

Littre's hernia is defined, with reference to his original description.

A case of Littre's hernia with spontaneous faecal fistula formation (the first recorded case of fistula in an inguinal hernia) is reported.

Cases of Littre's inguinal and femoral herniae (with and without faecal fistula formation) are reviewed.

Mention is made of the complications befalling Meckel's diverticula, and of the need for removing those diverticula incidentally found at laparotomy.

I thank Mr. G. C. Sawyer for permission to treat this patient and report the case. To him and to Mr. J. T. Rowling I am indebted for advice and assistance in the preparation of this article, and to Dr. R. Pigott and Mr. F. G. Saunders for the figures. My thanks are also due to Professor Ian Aird for his encouragement and help with the manuscript.

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TROPICAL HAZARDS ASSOCIATED WITH THE USE OF PENTACHLOROPHENOL

BY

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Nine deaths within a period of 18 months have occurred among workers in sawmills where pentachlorophenol ("santophen 20"), or its sodium salt, is used as a wood preservative. All these deaths were preceded by a peculiar illness which proved rapidly fatal, and, as details of intoxication do not appear to be widely publicized or well known, it was felt that this chemical is, in fact, more toxic than previously thought.

Properties and Local Use

The sodium salt (sodium pentachlorophenate; "santobrite") is readily soluble in water, stable, practically odourless, non-corrosive to metals, and toxic to a very wide range of micro-organisms, including fungi, yeasts, and bacteria. It is used in industry as a preservative, fungicide, and disinfectant, and in Sarawak is used mainly to prevent sap-stain in timber. Pentachlorophenol is not a scheduled poison and is often described as "relatively non-toxic." Although Edson (1955) listed it as "comparatively safe," he stated that as it was of recent introduction its comparative safety was provisional.

For the prevention of sap-stain it is used as a solution of between 1½ and 2% in water, and, on occasion, anhydrous sodium carbonate or borax is added to prevent acidic timbers causing precipitation of the pentachlorophenol with subsequent deterioration of its powers as a preservative of timber. During the rainy season, when sap-stain is especially prevalent, the concentration used is higher (2%) than during the dry season (1½%). The dip-tank is usually made of wood or metal, and is fitted with an inclined draining-board on to which the wood is pulled after being immersed in the solution in the tank. Two methods are in use: a mechanical method, where the wood is carried by an endless chain; and hand-

dipping, where the wood is lifted out by hand or by a wire hook. The wood rests approximately 30 to 60 seconds on the draining-board and is then lifted by hand on to trolleys and taken away for stacking. The wood is usually dripping wet with the solution and is often handled by men not wearing any protective clothing.

Clinical Details

The clinical details are given in Tables I and II. Sweating was pronounced in all cases. The most striking fact is the rapidity of the illness, with death ensuing within nine hours (in six cases) and within 16 hours in two (Nos. 2 and 4). In Case 9 the patient would, I think, have died within 12 hours had it not been for the most strenuous efforts to combat his hyperpyrexia and dehydration, which served to prolong his life for 25 hours from the onset of symptoms.

TABLE I

Case No.	Age	Date	Hyperpyrexia °F.	Hyperpyrexia °C.	Abdominal Pain of Nausea	Dyspnoea	Spasm	Hours from Onset to Death
1	19	15/10/53	104	40	Marked	Slight	Marked	3
2	20	26/2/54	105	40·6	Moderate	Marked	,,	13
3	22	16/3/54	102	38·9	,,	Slight	,,	3
4	30	14/5/54	104	40	Slight	Marked	,,	16
5	32	20/8/54	106	41·1	,,	,,	,,	6
6	25	10/10/54	101	38·3	None	,,	Unknown	9
7	17	12/3/55	101	38·3	Marked	,,	Marked	9
8	48	12/4/55	104	40	,,	Slight	,,	7
9	22	15/7/55	108	42·2	Slight	Marked	,,	25

TABLE II.—*Details of Cases*

Case No.	Post-mortem Findings	Chemical Analysis: Urine	Chemical Analysis: Organs	General Case Details
1	Inflamed gastric mucosa. ? Contamination by oral route	Not done	Not done	Had worked for 21 days on dip-tank. No gloves or protective clothing worn. Friends said he wiped his hands on paper before eating, but rarely washed
2	Inflamed gastric mucosa. ? Contamination by oral route	,,	Nil found	Worked for 21 days on dip-tank. No gloves or protective clothing worn. Was saving money and ate only one meal of rice a day
3	Nil abnormal discovered	,,	,,	Worked for 14 days on dip-tank. No gloves or protective clothing worn. Did not change clothes or wash when he finished work
4	Congestion of lungs noted. ? Inhalation contamination	,,	,,	Worked for 30 days on dip-tank. No gloves or protective clothing worn. Never washed or changed clothing when he finished work. Chain smoked cigarettes (home-made) while working
5	Nil abnormal discovered	,,	,,	Worked for 5 days on dip-tank. No gloves or protective clothing worn. Never washed or changed clothing when he finished work. Ate only one rice meal at 10 a.m. daily. Said he could not afford fish or meat
6	,, ,,	,,	,,	Worked for 7 days on dip-tank. Wore only rubber gloves and cotton shorts. Ate three meals a day but washed only at midday
7	,, ,,	Nil found	,,	Worked for 7 days on dip-tank. No gloves or protective clothing worn. Jumped out of boat on way to hospital as he was hyperpyrexial and thought he was going to die
8	Acute gastritis noted. ? Contamination by oral route	,,	,,	Worked for 8 days on dip-tank. No gloves or protective clothing worn
9	Acute oedema of brain and lungs. ? Inhalation contamination	P.C.P. 160 p.p.m.	,,	Worked for 3 days on dip-tank. Wore only rubber gloves and cotton shorts. Ate rice only twice a day as he was saving money. Rarely washed

Hyperpyrexia, gross dyspnoea, and prolific sweating were all noted, though abdominal symptoms were not such a marked feature as they were in the cases recorded in Australia by Gordon (1956). This might be explained by the local tolerance to abdominal symptoms, which are all too common a feature of the everyday life of these patients.

Terminal spasm was noticed in all cases, and was severe enough to be remarked on by relatives and lay attendants.

Case 9 is described in detail, as the signs, symptoms, and progress would appear to be characteristic of poisoning by pentachlorophenol.

Case 9

A male Sea Dyak aged 22, weight 115 lb. (52.2 kg.), worked at the dip-tank, sorting timber on the draining-board, for three days preceding his illness. He first complained of feeling unwell at 3 p.m. and of weakness in the legs; he vomited twice and had frequency of micturition. He then began to sweat copiously and became dyspnoeic. He was put in a boat and sent up-river to hospital by the hospital assistant, who was worried about the patient's condition, which appeared to be deteriorating rapidly. He arrived at hospital at 1 o'clock the following morning.

On examination he was conscious but could not give much in the way of a history and did not complain of anything very specific.

His temperature was 101.2° F. (38.4° C.), pulse 120, and respirations 35. He was sweating mildly, and clinical examination revealed very little that was abnormal, the main findings being considerable respiratory distress with respirations proceeding to Cheyne–Stokes type. The blood pressure was 75/50. The triceps-jerk in both arms and extensor plantar reflexes (bilateral) were absent.

An intravenous transfusion of glucose–saline and penicillin, 1 mega unit, was given prophylactically as he became comatose. He rapidly became hyperpyrexial in spite of the most strenuous efforts at sponging, fans, etc., and the rectal temperature was 105° F. (40.6° C.) 10 hours after admission. His coma deepened and he died 15 hours after admission without regaining consciousness. Terminally he had marked spasm of all his limbs and his rectal temperature was 108° F. (42.2° C.). Investigations gave the following results: Blood film for malaria parasites, negative; total white cell count, 13,870/c.mm.; red-cell count, 4,010,000/c.mm.; haemoglobin, 74% (Haldane); urine, trace of albumin; cerebrospinal fluid, normal pressure, N.A.D.

Post-mortem Examination.—Macroscopically the only abnormal findings were in the lungs, which were a bright red on section and were congested, but there was no evidence of pneumonia or infection. The spleen was chronically enlarged. Analysis of urine showed pentachlorophenol 160 ± 10 p.p.m. Histological report:—Brain: "Marked oedema; no cellular infiltration in the meninges or around the capillaries; nerve cells normal; no interstitial haemorrhage; no evidence of meningitis or encephalitis." Liver: "Architecture intact; no zonal necrosis or necrobiosis; slight fatty change." Lungs: "Marked oedema; no evidence of pneumonitis."

Treatment

The treatment of pentachlorophenol poisoning is very unsatisfactory and is largely symptomatic, the main points being to combat the hyperpyrexia, to replace the electrolytes, and to add glucose to replace the carbohydrate destroyed by pentachlorophenol's raising of the basal metabolic rate. Cortisone and chlorpromazine would theoretically be of benefit, but there is little clinical evidence to support this, though they are undoubtedly worth a trial.

Preventive measures, if rigorously applied, would seem to be the only answer at present, but they are very difficult to apply when dealing with superstitious and illiterate peoples. The diagnosis would appear to rest on awareness of the condition, together with the characteristic physical signs. Chemical analysis of organs or urine is extremely difficult and would often seem to be negative unless performed by laboratories well versed in the procedure.

Discussion

From the clinical details and the analysis of urine there would seem little doubt that the nine patients died of intoxication with pentachlorophenol. Lack of analytical evidence in Cases 1 to 7 can be partly explained by the fact that the analyses were performed in a small laboratory by a staff that did not have the facilities or the requisite knowledge to use an approved method for the estimation of pentachlorophenol.

The manufacturers (Monsanto Chemical Company, 1951) list the hazards of pentachlorophenol as being confined to irritation of the mucous membranes, sneezing, and contact dermatitis of exposed areas of skin, but various observers have noted toxic effects such as peripheral neuritis. Campbell (1952) described several cases of polyneuritis in men and women who had used a preparation for treating woodworm which contained pentachlorophenol.

In Germany peripheral neuritis, mucosal irritation of the upper respiratory tract, and acne were described by Baader and Bauer (1951).

Animal experiments, however, gave the impression that when lethal doses were administered the symptoms were extremely rapid in onset and included fever and toxaemia (Carswell and Nason, 1938), while Brune *et al.* (1954) described the hyperthermia and raised metabolic rate in animals who were poisoned with pentachlorophenol. Truhaut *et al.* (1952b) noted this also, and described two fatal cases (Truhaut *et al.*, 1952a) in France in which the clinical picture was one of sudden rise in temperature to great heights, profuse sweating, suffocation, muscular contraction, with death supervening in less than 24 hours.

Nomura (1953), in Japan, described a fatal case and two non-fatal cases, and it was noted that the weather was very hot at the time. Profuse perspiration was again a marked symptom.

Gordon (1956), in Australia, has described nine cases, of which five proved fatal. In eight of these sweating and fever were noted, and in two of the fatal cases there was marked spasm. The deaths were all within 30 hours of the onset of symptoms. Only in the last case did analysis reveal the presence of pentachlorophenol.

Edson (personal communication) has expressed the view that pentachlorophenol, like dinitrophenol and dinitrocresol, causes a radical uncoupling of oxidation and phosphorylation cycles in the tissues, thus producing a marked increase in basal metabolic rate with all the effects of heat accumulation.

Local Factors

Sarawak has a humid tropical climate, the temperature rarely falling below 70° F. (21.1° C.) or rising above 90° F. (32.2° C.), and with an annual rainfall of 150 in. (380 cm.). The sawmills are mainly situated down-river between 60 and 90 miles (96 and 145 km.) away from the nearest hospital or doctor. Transport is almost entirely by small boats, powered by outboard motors, and, owing to the vast size of the rivers, and the driftwood on them, travelling is limited to the hours of daylight. An unexplained feature of the illness has been its predilection for the true native races (Dyak, Kayan, etc.) rather than the Chinese or Malays, even though there are as many, if not more, of the latter working on the same job. In every instance the Dyaks involved have been men from "up-river" who had come down to the coastal areas as seasonal workers. As physical types they are not very impressive—height around 5 ft. 4 in. (162 cm.), weight 100 to 110 lb. (45.4 to 50 kg.), and mostly suffering from mixed worm infestations (*Ancylostoma duodenale* and *Ascaris*) and malaria. Their diet is in almost every case a straight rice diet, with little or no protein foods. They are a highly superstitious people given to having dreams and being talked into sickness.

The normal clothing worn by workers in Sarawak consists of only a pair of cotton shorts, and it is likely that gross contamination occurred, especially as in the early days of the use of pentachlorophenol few workers wore rubber gloves, aprons, or boots. Washing rarely involves the use of soap, and normally consists of immersion (wearing the shorts) in one of the large rivers that abound here. In addition, owing to poor supervision, the strength of the solution in the dip-tank rises to unknown values because of the addition of fresh stock solution at periodic intervals without the prior removal of the sludge from the bottom of the tank. A further hazard is due to the fact that Dyaks and Kayans eat their food with their hands, which are apt to be grossly contaminated. Chinese who work in the same conditions, wearing similar clothes, appeared to be immune from the toxic effects, probably because of their better physique, superior diet, and greater care in attending to personal cleanliness.

An interesting sidelight on personal immunity is provided by an Australian overseer of very powerful physique, who, to convince the Dyaks that the solution was not a poison, drank a glass of the 2% solution from the tank. He is reported to have stated that, apart from a severe hangover, he was unaffected.

Since these deaths, strict precautions have been insisted on; these include the prohibition of employment of natives on the dip-tank, rotation of workers so that no one works more than 14 days on the tank, the wearing of rubber gloves, aprons, and boots, the provision of washing facilities next to the tank so that frequent washing can take place, and the reduction of the strength of the solution used to a maximum of 2% (borax being added to keep the solution alkaline when used with acidic timbers). In addition, workers are required to drink a pint of milk a day.

As a result of these measures no deaths or serious cases have been reported in the past 18 months.

Summary

Nine cases of unusual illness are recorded, and, in one, pentachlorophenol was found in high concentration in the urine. The illnesses were characterized by signs of a raised basal metabolic rate, and it is suggested that they were due to poisoning with pentachlorophenol.

The difficulty of accurate diagnosis at the time, owing to lack of any simple specific test, and the need for chemical analysis to be carried out at specialized centres, is stressed. Post-mortem macroscopic and microscopical findings have not so far revealed any diagnostic lesions.

It is also suggested that the problem may well be magnified in tropical countries where workers live on a simple rice diet and may have some racial susceptibility.

My thanks are due to the Director of Medical Services, Sarawak, Dr. W. Glyn-Evans, for permission to publish these cases and to Dr. E. F. Edson for his invaluable help and encouragement in elucidating this problem.

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PROTEIN CONTENT OF OEDEMA FLUID IN LYMPHOEDEMA

BY

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Lymphangiography (Kinmonth *et al.*, 1955, 1957) has demonstrated the structural defects of the lymphatic system in primary lymphoedema. This report is concerned with some of the physiological disturbances caused by lymphatic malfunction in patients with primary lymphoedema.

Method.—Oedema fluid was obtained from the subcutaneous tissue of patients suffering from chronic primary lymphoedema of the legs. A small-bore Southey tube was used to collect the fluid, and a sufficient quantity was obtained to enable the total protein concentration to be estimated by a biuret method in 38 patients. In addition, the albumin/globulin ratio and the paper electrophoretic pattern of this protein was determined in 20 patients. The majority of patients were ambulant up to the time of collection of the sample of oedema fluid.

Results

Protein Content of Oedema Fluid.—Fig. 1 shows the protein level of the oedema fluids from 38 patients with primary lymphoedema. The patients are grouped into three

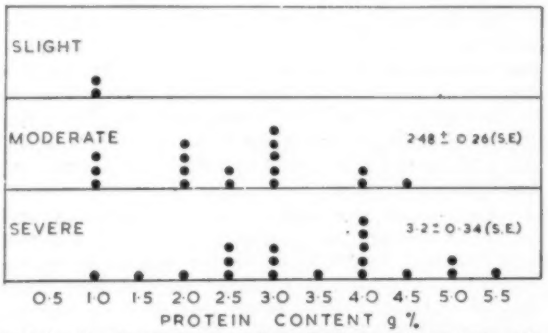

FIG. 1.—Protein content of oedema fluids from 38 patients with primary lymphoedema. Protein level for each patient is charted individually to nearest 0.5 g. Mean values for moderate and severe groups are indicated at right of chart.

categories according to the clinical degree of their oedema. The mean protein content of the oedema fluid for the whole group was 2.8 g. per 100 ml. The protein levels ranged from 1 to 5.5 g. per 100 ml., and the series as a whole would fit into the high protein category of oedema fluid as proposed by Crockett (1956). Fluids with the highest levels of protein tended to be found in patients with severe clinical disease, although the mean values of the moderate and severe groups of patients did not differ significantly.

Albumin/Globulin Ratios.—The A./G. ratios in the sera and oedema fluids of 20 patients were determined, and are shown plotted against one another in Fig. 2. For most patients the A./G. ratio was higher for the oedema fluid than for the serum, the mean difference being 1.2 ± 0.44 (S.E.), which is significantly greater than zero at the 5% level ($t=2.72$, $n=19$, $0.01<P<0.05$). The theory of restricted diffusion (Pappenheimer, 1953) implies that the ability of protein molecules to pass through the normal capillary wall varies inversely with their size. The small albumin molecules have least difficulty in negotiating the molecular sieve of the normal capillary wall, and their relative concentration rises in the oedema fluid. Albumin

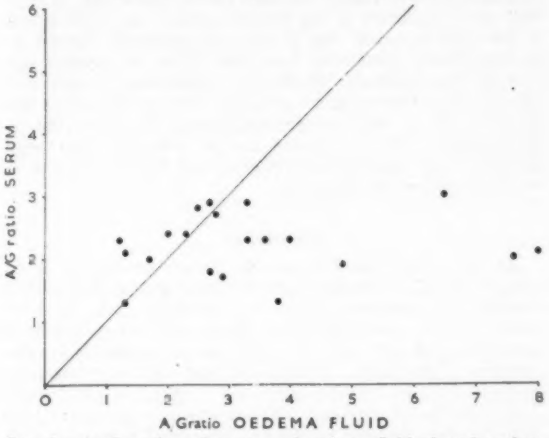

FIG. 2.—A./G. ratios of serum and oedema fluid plotted against one another in 20 patients and lymphoedema. Each patient is charted individually, and in those falling to the right of the oblique line the A./G. ratio was increased in oedema fluid.

molecules are osmotically more active than the other components of the plasma proteins, and their increased preponderance in the oedema fluid will increase the magnitude of the physiological disturbance.

Electrophoresis.—The electrophoretic pattern of the oedema fluids differed consistently from that of their parent sera in that the α_2-globulin fraction was either absent or greatly diminished (Fig. 3). This relative absence is

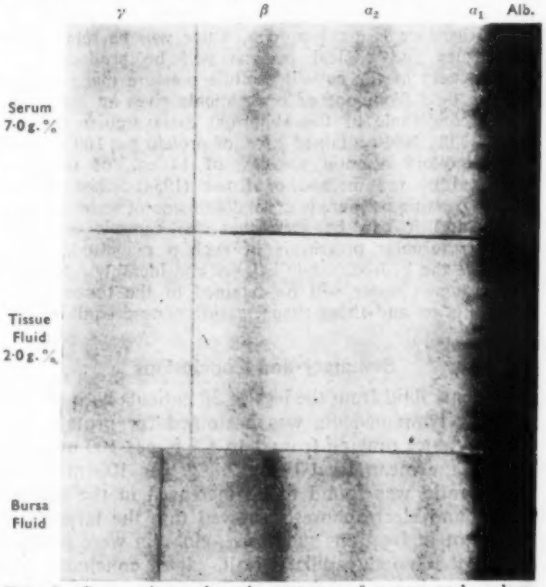

FIG. 3.—Paper electrophoresis patterns of serum and oedema fluid from a patient with lymphoedema, and of fluid from an inflamed bursa. The α_2-globulin band is greatly diminished in oedema fluid.

probably due to the large molecular size of the α_2-globulin, which would encounter considerable physical restriction in diffusing through the normal blood capillary wall. The significance of this observation and that of the increase in

albumin concentration in the oedema fluid lies in their indication that blood capillary permeability remains unaltered in uncomplicated lymphoedema. Pathological processes, such as inflammation, which render the capillary wall abnormally permeable produce extravascular fluids that have an electrophoretic pattern resembling closely their parent serum. Fig. 3 includes the electrophoretic pattern of fluid obtained from a slightly inflamed bursa, and it can be seen that all components of the plasma protein are represented. It was also observed that in the electrophoretic pattern of oedema fluids containing less than 2.5 g. of protein per 100 ml. the β-globulin band was a prominent feature and second only to albumin in intensity. It is probable that this band is due to the iron-binding globulin (siderophyllin or transferrin). This substance has a molecular size only slightly larger than that of albumin, and has been found in nephrotic urine (Neale, 1955).

Discussion

An important function of the lymphatic system is to remove protein molecules from the tissue spaces. Lymphatic insufficiency interferes with this function, and we have shown (Taylor *et al.*, 1957) that plasma proteins are removed abnormally slowly from the subcutaneous tissues in lymphoedema. On these grounds it can be expected that oedema fluid in lymphoedema will contain an abnormally high quantity of protein. The investigation presented here confirms this, and the results are in general agreement with the observations of Drinker *et al.* (1934) on four patients, Watson (1953) on five patients, and Crockett (1956) on 10 patients with lymphoedema.

The Starling hypothesis (Starling, 1896) of tissue-fluid formation depends on the high protein content of the plasma to provide an osmotic force sufficient to promote absorption of tissue fluid into the vascular bed at the venous end of the capillary loop. In lymphatic insufficiency the small quantity of plasma protein that normally leaks through the capillary wall will accumulate in the tissue spaces. This extravascular protein then exerts an osmotic pressure in opposition to that of the plasma protein, and in consequence absorption of water from the tissue spaces is impaired. If the disturbance is great enough, water will be retained in the tissues and clinical oedema will be produced. A measurement of the colloid osmotic pressure made on the oedema fluid from one of our patients gives an indication of the magnitude of the abnormal extravascular osmotic force. This fluid contained 2.5 g. of protein per 100 ml. and had a colloid osmotic pressure of 14 cm. of water as measured by the method of Rowe (1954). The plasma colloid osmotic pressure is normally 36 cm. of water (Landis, 1934), and it can be seen that the osmotic force of the extravascular protein is of such a magnitude as to influence the hydrodynamic balance considerably. In these circumstances water will be retained in the tissue spaces until dilution and rising tissue tension restore equilibrium.

Summary and Conclusions

Oedema fluid from the legs of 38 patients with chronic primary lymphoedema was examined for protein content. Values ranging from 1 to 5.5 g. per 100 ml. were found, the mean level being 2.8 g. per 100 ml. The A./G. ratio was found to be increased in the oedema fluids, and electrophoresis showed that the large-molecule protein fractions such as α_2-globulin were retained inside the blood capillary wall. It is concluded that lymphatic failure results in an accumulation of protein molecules in the tissue spaces and that water retention and oedema are produced by this abnormal extravascular osmotic force. Capillary permeability is unaltered in uncomplicated lymphoedema.

We thank Mr. M. P. Curwen for statistical advice, Dr. D. S. Rowe for the measurements of osmotic pressure, Dr. E. Smith for assistance with the electrophoresis, and Miss D. Aitken for technical assistance. The investigation was done during the tenure of a B.M.A. scholarship held by one of us (G. W. T.).

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TREATMENT OF FAT EMBOLISM WITH HEPARIN

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Aird (1949), writing of fat embolism, states that "most patients who suffer from fat embolism probably recover, but those in whom the diagnosis is made during life usually die." Faced with a severe case of this condition in 1956, one of us (R. H. S.) consulted the Department of Pharmacology of the University of Birmingham and was advised to try the use of heparin. This patient recovered, and heparin has since been used successfully in two further cases.

The pharmacological basis of the treatment is the effect *in vivo* of heparin "clearing" lipaemic plasma—that is, rendering translucent plasma which has become opalescent after a fatty meal (Hahn, 1943). French, Robinson, and Florey (1953) suggested, therefore, that the fat globules present in the blood of patients suffering from fat embolism might be similarly lysed, reducing the risk of infarction.

As a result of experiments with the heparin treatment of artificially induced fat embolism in rats, Gardner and Harrison (1957) came to the conclusion that a clinical trial of heparin in human fat embolism would not be justified. They found that, in their animals, heparin both accelerated death and increased the number of deaths after fat embolism. In view of these findings we present below three human cases in which heparin was successfully used. Despite the view of de Takáts (1945) that there may be regression of symptoms to complete recovery, no matter how serious the initial symptoms, these three were of such severity that we would otherwise have expected them all to be fatal.

Case 1

A soldier aged 23, a pillion passenger on a motor-cycle, received a closed fracture of the mid-shaft of the right femur on May 15, 1955. This was treated by extension, with a Steinmann pin through the tibial tuberosity, on a Thomas splint. No blood transfusion was given at this stage. On the evening of the 16th his temperature was 101.6° F. (38.7° C.), but the pulse and respirations were normal. On May 17 his temperature was 102.8° F. (39.3° C.), pulse 86,

and respirations 20. Pneumonia was suspected and penicillin, 300,000 units six-hourly, was started by intramuscular injection. On May 19 there was dullness on percussion of the left side of the chest compared with the right, and numerous rales were heard at the left base. Next day the patient was drowsy and complained of headache; dyspnoea and slight cyanosis were present, with blood-stained sputum. The chest moved freely, but rales were still present at the left base. The optic fundi showed small haemorrhages in the right retina, and petechial haemorrhages were present in both supraclavicular fossae.

Chest *x*-ray examination on May 20 showed: "Portable film compatible with extensive fat embolus of lungs. No *x*-ray evidence of left rib fractures." The urine examined the same day contained no fat globules. Report on sputum: "There are fairly numerous fat globules measuring up to 30 microns in diameter. This is said to be an invariable finding in fractures of marrow bones." A diagnosis of fat embolism was accepted, and the fracture was relegated to second importance.

On May 20 aminophylline, 3 gr. (0.2 g.), was given intravenously, together with heparin, 12,500 units intravenously, in the morning. A further 25,000 units of heparin was given intramuscularly that night. Next day aminophylline, 3 gr. (0.2 g.) four-hourly, was given orally, together with heparin, 25,000 units intramuscularly, at 6 p.m. A clotting-time estimation done just before this injection was reported as 6 minutes. On May 22 a further 25,000 units of heparin was given. The patient's condition remained critical for some days, but by June 1 he had so improved that open reduction and plating of the fracture was carried out and a plaster-of-Paris case was applied. *X*-ray examination on September 30 (13 weeks after the plating operation) showed union so advanced that a walking-calliper was fitted. There was considerable swelling of the calf and foot, and the knee was stiff. The calliper was finally discarded on April 23, 1956. By June there was 90 degrees flexion at the knee-joint; the thigh and leg had no swelling. The patient was back at civilian work and was able to take part in all reasonable activities.

Case 2

A man aged 40, involved in a motor-cycle accident, received multiple laceration, a closed but grossly comminuted fracture of the left femur, and an open fracture of the left tibia and fibula. There was no head injury. Two pints (1,140 ml.) of blood was given, the fractured tibia reduced and plated, and a Steinmann pin inserted through the tibial tuberosity for extension of the fractured femur. Two days later he became collapsed and mentally confused. He was incontinent of urine and had purpuric spots on the upper chest and the shoulders. A portable *x*-ray film of his chest on this day "failed to reveal any gross pulmonary pathology."

A clinical diagnosis of fat embolism was made, and treatment with heparin, 4,000 units intravenously four-hourly, plus aminophylline, 0.2 g. intravenously four-hourly, was begun, and continued for 48 hours. On the day after treatment was begun the injured thigh was grossly swollen and bruised, due obviously to bleeding at the fracture site, and this was the main factor in limiting the duration of heparin treatment to two days. Rapid improvement in the general condition occurred, and by the eighth day after the accident the patient's condition was back to that of the first day. Union of the two fractures was delayed, the femur taking nine months and the tibia fifteen. He did not resume work for a further six months owing to stiffness of the left knee-joint.

Case 3

A man aged 19 received an open oblique fracture of the mid-shaft of the right tibia and fibula while playing football; there was no other injury. Surgical toilet and reduction were performed within a few hours of admission and a full-length plaster-of-Paris case was applied. Three days later he became drowsy and cyanosed, with a temperature of 100° F. (37.8° C.). There was no cough and the chest was clear; the wound showed nothing abnormal. Within a few hours a physician found "some patchy consolidation—rales mainly in the right base zone. No tracheal displacement. Rapid breathing. Temperature 100° F. (37.8° C.), pulse 130. Fairly profuse petechial rash on neck and shoulders. Semi-stupor without localizing neurological signs. Optic disks: no evidence of fat embolism here." Urine taken at this stage was subsequently reported to contain no fat droplets and a blood culture was negative. A clinical diagnosis of fat embolism was accepted and treatment with oxygen and penicillin was begun. Heparin, 12,500 units intravenously followed by 25,000 units intramuscularly twice daily, and aminophylline, 0.5 g. intravenously six-hourly, were given for three days. At the end of this time there was marked improvement in the general condition and no bleeding at the fracture site occurred.

Portable *x*-ray film of the chest on the sixth day after injury showed: "Increased transverse diameter of the heart, especially left ventricle. The lung fields appear to be clear." The serum total lipid fatty acid+cholesterol= 505 mg./100 ml. (normal) on the same day.

On the 18th day after the accident a Steinmann pin was inserted through the os calcis for extension, and a plaster-of-Paris case was applied. Union of the fracture was complete and the plaster-of-Paris was removed at the 19th week. Rehabilitation was slow, and at the 10th month, when the patient was discharged, there was still some stiffness of the foot.

Comment

The treatment with heparin of three patients whose fractures were complicated by the occurrence of fat embolism is reported. Unfortunately the diagnosis in each case was made on clinical grounds only, but this was largely because it was considered to be so clear. The dosages of heparin employed were those used in deep calf-vein thrombosis, and, although the records of clotting-time are not available, it was raised considerably in each case. The shortness of the course given—that is, three days in each—is noteworthy. Haemorrhage at the fracture site, delayed union, and more than usual joint stiffness after conventional treatment of the fracture were noted. The latter complication is possibly due to the forced neglect of physiotherapy in the early days after injury, when the general condition of the patient is so poor.

Summary

Three patients with severe fat embolism, all of whom might have been expected to die, recovered after treatment with heparin.

It is suggested that heparin treatment is worthy of further trial in this serious condition, and that a controlled series of cases would be justified.

We are grateful to the surgeons concerned for permission to publish their cases, and to the Misses G. Gaughan and S. Gamble for secretarial assistance.

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Volume II of the *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death* (Seventh Revision) has now been published by the World Health Organization, Geneva. It contains alphabetical indexes to the terms used in volume I, which was reviewed in the *Journal* of January 11, 1958 (p. 94). Both volumes are obtainable from H.M. Stationery Office, price 35s. the set.

Medical Memoranda

Adrenal Apoplexy

Massive bilateral adrenal haemorrhage is best known as it occurs in the involuting adrenal cortex of newborn infants or as a complication of meningococcal septicaemia in children and young adults. In other settings, such as pregnancy (Keele and Keele, 1942; Crawford, 1951; Dewhurst, 1951) and toxaemic illness (Wilson and Roth, 1953; Owen and Coleman, 1955), the adrenal lesion may escape recognition if its manifestations are unfamiliar to the clinician. The symptoms and signs of adrenal apoplexy appear in pure form when the patient is struck down while apparently enjoying normal health. The following example of adrenal apoplexy is reported in order to draw attention to the characteristic clinical features, and to emphasize the need for early diagnosis now that cortisone therapy offers hope of survival to these patients.

CASE HISTORY

A man of 62 suffered from chronic bronchitis, and for some years had been breathless on exertion. He had experienced two asthmatic attacks in the six months before his final illness, and was in the habit of administering to himself 5 min. (0.3 ml.) of hyperduric adrenaline twice daily. Whilst in his usual state of health he developed some upper abdominal discomfort, which was followed in a few hours by severe upper abdominal pain. He vomited once after a Seidlitz powder taken in the hope of obtaining relief.

On admission to hospital a few hours after the onset of the acute pain, he was pale and restless, breathing with difficulty, and greatly distressed by upper abdominal pain, which was aggravated by coughing and varied in intensity, but was not colicky and did not radiate. His temperature was 97° F. (36.1° C.), pulse 80, respirations 24, and blood pressure 180/100 mm. Hg. The abdomen was not distended, and moved freely in all quadrants. On palpation the lower abdomen was quite soft, but firm pressure revealed tenderness and slight resistance in both subcostal regions and to a less degree in the epigastrium. Bowel sounds were few and faint, but *x*-ray examination revealed neither bowel distension nor gas in the peritoneal cavity. Since there was no indication for immediate laparotomy a stomach tube was passed and hourly aspiration instituted.

The next day he was given water in 1-oz. (28-ml.) feeds, and very little of it was returned by the gastric tube. His general condition had not improved and the pain was not relieved by pethidine given in 50-mg. doses four-hourly. The following morning the pain abated slightly, but at midday the temperature rose to 100.5° F. (38° C.), the pulse to 110, and the respirations to 35. At this time the blood pressure was 160/98 mm. Hg, but six hours later it fell and became unrecordable, and the pulse rate rose to 130. The patient lingered for some hours in a state of deepening shock, and finally died, approximately 54 hours after the onset of his symptoms.

Necropsy Findings.—The main lesion was found in the adrenals. Each gland was enlarged to several times its normal size by blood clot, which occupied the medulla and extended irregularly into the cortex. The blood clot was enclosed by a rim of yellow cortex measuring in most places 2–3 mm. thick. Extravasated blood also infiltrated the periadrenal tissues, particularly on the left side, and made it difficult to determine the state of the main adrenal veins. The terminal portion of the right adrenal vein, however, was identified and found to be free of thrombus up to its junction with the inferior vena cava. No haemorrhages were found elsewhere in the body or on the skin surface. The only other noteworthy findings were pulmonary emphysema, and dilatation and slight hypertrophy of the right ventricle of the heart, which weighed 300 g.

Microscopical Examination.—The histological picture was the same in both adrenal glands. The medulla and, to a less extent, the inner portions of the cortex were destroyed by haemorrhage. The outer part of the cortex was congested and patchily haemorrhagic, but was free from obvious necrosis. The central medullary vein and its tributaries were full of thrombus of such recent formation that it was impossible to tell whether it had formed before or after the haemorrhage.

DISCUSSION

Bilateral adrenal apoplexy in apparently healthy persons (Pearl and Brunn, 1928; Hall and Hemken, 1936; Barsoum, 1936) and in individuals with only minor disabilities (Lavenson, 1908; MacMillan, 1947) has most often been attributed to thrombosis of the adrenal veins. Thrombus was undoubtedly present in the medullary veins in our case, but, as in MacMillan's case, it was of such recent formation that it was impossible to tell whether thrombosis had preceded or followed the haemorrhage. Pulmonary and systemic hypertension may have been concerned in the pathogenesis, since adrenal haemorrhage has been observed in a number of cases of chronic cardiac or pulmonary disease with venous congestion (Lavenson), and has been reported in association with asthma (Lavenson) and hypertension (MacMillan).

Keele and Keele made a particularly careful analysis of the symptomatology of adrenal haemorrhage. Their review, and study of other reports, make it clear that the clinical picture is characteristic.

Pain may be agonizing from the onset, but more commonly increases to maximum severity in a few hours, and may abate somewhat after two days. It is commonly described as stabbing or tearing, and may vary in intensity, but is never colicky. It is felt most often in the subcostal region on the side of the affected gland, but may be referred to the midline above the umbilicus or, less commonly, to the back in the kidney region. In their case of right-sided adrenal apoplexy Keele and Keele localized the pain to an area about the size of a half-crown situated to the right of the umbilicus about 2 in. (5 cm.) below the costal margin. They interpreted it as a referred pain in the 10th thoracic segment, arising either from afferent stimuli from the adrenal medulla or from retroperitoneal irritation. MacMillan has suggested that stimulation of sensory-nerve endings in the tense adrenal capsule could cause pain in thoracic segments 5–10, and this may explain the more diffuse distribution of the pain in some cases. Tenderness is usually present in the subcostal region on the affected side: it may also be present in the renal angle or epigastrium with or without subcostal tenderness. Rigidity is unusual, but may develop in the upper abdomen on the affected side. Vomiting is a common early symptom, and may be severe.

Other Symptoms and Signs.—Restlessness and sweating are almost invariable in the early stages. The temperature, the pulse, and respirations may be relatively normal at the onset, but increase later. The blood pressure is usually well maintained until the terminal stages of the illness. Leucocytosis has been pronounced in several cases. Most of the characteristic symptomatology was present in our case, but the vomiting was not severe, and did not recur after gastric aspiration. The severity of the pain, the relative insignificance of the abdominal signs, and the complete lack of response to early conservative measures made it clear that this grave illness was no ordinary abdominal emergency.

The natural course of the disease in some cases has been modified by laparotomy, but when this is not done there may be little change in the patient's condition for 36 to 48 hours. After this time, falling blood pressure and mental clouding indicate the onset of acute adrenal insufficiency; deterioration is then rapid, and death is not long delayed.

The temporary postponement of acute adrenal insufficiency after adrenal apoplexy recalls the sequence of events following extirpation of the adrenals in dogs. It is the most hopeful feature of the condition in that it allows time for the institution of cortisone therapy. The clinical features of the disease appear to be distinctive enough to allow of pre-operative diagnosis, but should a laparotomy be performed for symptoms of this nature, then negative abdom-

inal findings should prompt the examination of the more accessible left adrenal region before the abdomen is closed.

We are indebted to Mr. T. I. Wilson and Mr. A. Barron, surgeons to Leith Hospital, for permission to publish the clinical details of this case, and to Dr. J. M. Drennan, consultant pathologist, Edinburgh Northern Hospital Group, for constructive criticism.

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Rovsing's Sign

In 1956 Davey reported a study of Rovsing's sign (Rovsing, 1907, 1908) based on a series of 303 consecutive cases of acute appendicitis. He found the sign in five cases. In an earlier study Yasui *et al.* (1953) failed to elicit the sign in any of 354 cases of acute appendicitis. This discrepancy is here examined.

At the time of operation we inserted a large-gauge needle (1 mm. diameter) into the caecum and attached to it a rubber balloon or a kymograph. On compressing the descending colon no intracaecal rise of pressure was observed even when the terminal ileum was clamped. Next a barium enema was given, and, after it had been confirmed by screening that the contrast medium extended to the middle of the ascending colon, antiperistaltic pressure was applied in the left iliac fossa : no change was observed in the caecum and there was no movement of the contrast medium towards it.

Tests in cadavers gave similar results ; although, if the colon was inflated with gas to five or ten times its normal size and thus converted into a single continuous tube, Rovsing's theory became true. But this would not happen in the living subject. From these observations, therefore, it seems reasonably certain that Rovsing's sign cannot occur in acute appendicitis.

ROVSING-LIKE SIGN

During this three-year investigation we encountered in 14 cases a sign rather similar to Rovsing's sign. In these cases (Table I) the sigmoid colon was either lying in direct contact with the inflamed appendix or attached to it by fibrinous adhesions. When the left iliac fossa was compressed the irritable appendix was rubber or dragged upon by the sigmoid colon and pain resulted. The sign was also observed in cases without appendicitis where the sigmoid colon was distended with gas or faeces. In these cases the sign elicited less pain (Table II), and was probably due to direct compression or traction of the sigmoid itself.

COMMENT

Davey (1956) concluded that Rovsing's sign was uncommon, that when present it indicated an inflammatory lesion in the right iliac fossa lying in direct contact with the parietal peritoneum, and that the probable cause of the pain was a momentary vibration or displacement of the abdominal wall or abdominal contents leading to friction between the inflamed viscus and the overlying anterior parietal peritoneum. To call the sign occurring by such a mechanism Rovsing's sign seems somewhat inappropriate. Davey's explanation of it is very similar to that of Lauenstein (1908, 1911), Hofmann (1908), and Hausmann (1911). Rovsing's sign in the true sense would be one in which abdominal pain in the right iliac fossa resulted from an antiperistaltic movement of colonic contents initiated by compression of the left iliac fossa. But this, as already shown, is impossible in the living subject with acute appendicitis.

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TABLE I.—*14 Cases with a Rovsing-like Sign*

Case No.	Diagnosis	Age and Sex	Rovsing-like Sign	State of Appendix	Pathological Anatomy of the Sigmoid Colon	Remarks
1	Appendicitis	26 F	±	Catarrh	In direct contact with inflamed appendix, but not adherent; slightly elongated and mobile	Appendicectomy
2	Appendicular colic	21 F	±	No inflammation	In direct contact with appendix, inflated with gas	,,
3	Appendicitis	19 M	+	Gangrene extending to caecum	In direct contact with appendix, inflated with gas	,,
4	Caecum mobile; sigmoid elongated and mobile	17 F	+	No inflammation	Elongated, mobile, inflated, and filled with faeces	Laparotomy as acute abdomen; appendicectomy and sigmoidectomy
5	Appendicitis	21 M	+	Catarrh	In direct contact with inflamed appendix	Appendicectomy
6	Caecum mobile; sigmoid elongated and mobile	21 M	±	Already removed	In direct contact with caecum, atonic, and inflated with gas	Sigmoidectomy, caecoplication
7	Appendicitis	22 F	+	Catarrh	Overlying caecum and appendix	Appendicectomy
8	,,	19 F	+	Abscess formation	In direct contact with appendix	Appendicectomy, caecoplication
9	Circumscribed peritonitis due to appendicitis	49 M	+ +	Gangrene	Adherent to inflamed appendix and caecum	Appendicectomy
10	Circumscribed peritonitis due to appendicitis	39 M	At first inspection + +	Post-inflammatory scarring	Adherent to appendix	Appendicectomy 25 days after admission
11	Appendicitis; caecum mobile; sigmoid elongated and mobile	21 F	±	Catarrh	In direct contact with appendix	Appendicectomy
12	Appendicitis	25 M	+	Gangrene	In direct contact with appendix	,,
13	,,	50 M	+ +	Purulent	Adherent to appendix	,,
14	Appendicitis; intestinal stenosis due to inflammatory adhesion	37 F	+ +	Perforated	Inflammatory hypertrophy and adherent to apex of appendix	Diarrhoea and severe tenesmus prior to operation; appendicectomy, and sigmoidectomy

TABLE II.—*Severity of Pain in Rovsing-like Sign Related to Diagnosis*

Diagnosis	Severity of Pain			Total
	Severe	Moderate	Mild	
Appendicitis	2	5	2	9
Circumscribed peritonitis due to appendicitis	2	0	0	2
Appendicular colic	0	0	1	1
Mobile caecum, and elongated and mobile sigmoid	0	1	1	2
Total ..	4	6	4	14

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Reviews

CHEST COMPLICATIONS OF ABDOMINAL SURGERY

Pulmonary Complications of Abdominal Surgery. By Anthony R. Anscombe, M.S., F.R.C.S. (Pp. 121+x; illustrated. 20s.) London: Lloyd-Luke (Medical Books) Ltd. 1957.

This is an excellent physiological and clinical study of a problem which frequently troubles both surgeon and anaesthetist. Though the mortality from pulmonary complications following abdominal operations has undoubtedly diminished, yet the author states, and presents figures which support his statement, that "the incidence of post-operative pulmonary complications has altered but little during the last forty years." The surgeon may be surprised, and he will find little comfort in the further dictum that "the anaesthetic and the method of administration have no significant effect on the incidence of pulmonary complications."

After a thorough investigation of the whole problem the decision is reached that "the chief interference with pulmonary mechanical function is a protective reflex from the anterior abdominal wall." This reflex varies according to the position and size of the incision, and the relative merits of various incisions are usefully discussed. The author sees danger in keeping the patient in the Trendelenburg position for a prolonged period. He is in favour of breathing exercises after operation and assesses the value of post-operative physiotherapy. He sees no harm and some benefit in the giving of small doses of morphine to relieve pain after operation. Finally a challenge is thrown down. "It is suggested that the investigation of pulmonary mechanical efficiency is as essential as the knowledge of the haemoglobin and blood group of a patient who is to undergo an abdominal operation. The vital spirogram is at present the best test available." What the vital spirogram is the reader must find out for himself by reading the book. It will repay him.

ZACHARY COPE.

INTRODUCTION TO PAEDIATRICS

A Primer of Paediatrics for the Senior Student and Family Doctor. By Elchon Hinden, M.D.(Camb.), M.R.C.P.(Lond.). Foreword by Kenneth H. Tallerman, *M.C.*, M.D., F.R.C.P. (Pp. 356+xv. 25s.) London: Macdonald and Co. 1957.

Dr. Hinden set himself a difficult but very worth-while task when he planned this book, which is intended primarily for senior medical students and family doctors. His object was to present a picture of "the common things the family doctor will encounter in his young patients" and to set them against the background of healthy childhood, describing the successive stages of a child's life, his gradual development, and the characteristics of his progress. To adopt this chronological approach necessitates—as the author acknowledges—a certain amount of repetition, which is no handicap if the book is read, as one would read a novel, from cover to cover. But it is to be hoped that Dr. Hinden will include an index in subsequent editions for the benefit of those who wish to refer again to particular subjects, and cross-references would be helpful.

The book is divided into three sections covering the age periods from conception to 4 weeks, from 4 weeks to 2 years, and from 2 years to puberty. Each section deals with normal growth and development during the period under consideration, and then describes fairly systematically the common diseases that tend to present themselves during the period. It is a question whether Dr. Hinden's brief references (often only by name) to so many comparatively rare conditions have not clouded his avowed intention of maintaining a proper balance between the common and the unusual. It is also questionable whether the author's chatty style of writing is the most suitable for medical students, who still have their examinations before them. On the other hand, qualified doctors will welcome an approach that is forthright as well as breezy, and they will enjoy assessing Dr. Hinden's dogmatism in the light of their own experience. The fundamental idea of this book has been to focus the reader's attention upon the child as an individual rather than a patient suffering with this or that disease. It is a move in the right direction.

NORMAN B. CAPON.

CONNECTIVE TISSUE

Connective Tissue. A Symposium Organized by the Council for International Organizations of Medical Sciences. Edited, under the direction of R. E. Tunbridge, by Madeline Keech, J. F. Delafresnaye, and G. C. Wood. (Pp. 371+xii; illustrated. 42s.) Oxford: Blackwell Scientific Publications. 1957.

In July, 1956, the Council for International Organizations of Medical Sciences held a symposium in London which was attended by most of the chemists, physicists, and medical men who have contributed to our knowledge of the biochemistry and structure of connective tissue. The proceedings of this meeting are here published under the editorial direction of Professor R. E. Tunbridge, who presided. Each contributor gives a short account of recent research followed by an exposition of current hypotheses—this is always most convincing until one reads the critical comments made by the other experts. These corrective remarks are invaluable to the inexpert, since they show what is generally acceptable and what is not.

The structure of collagen is discussed by such experts as W. T. Astbury, R. S. Bear, R. Reed, W. Grassmann, W. Schwarz, and F. Verzár. The picture that emerges is of a basic protofibril composed of three polypeptide chains wound round each other in a coiled triple helix. These protofibrils are in turn twisted together to form the familiar cross-striated fibrils seen on electron-microscopy. At yet a higher level the anatomical tendon bundles also show a coiled structure. Thus the nice straight tendon fibre is really a fantastically twisted structure like some gigantic rope. K. H. Gustavson marshals convincing evidence for the importance of hydroxyproline in stabilizing the collagen fibre, and we can now contemplate the fascinating possibility of our collagen becoming unravelled through failure of some simple chemical reaction such as the hydroxylation of proline. Chemical evidence concerning the precise sequence of various amino-acids in the peptide chain of collagen is presented by W. Grassmann, and it seems likely that all the details of the collagen molecule will be worked out before long. Collagen metabolism is discussed by D. S. Jackson, J. Gross, and V. N. Orekhovitch. All are agreed that, although the main mass of collagen is metabolically inert, there is a highly active and more soluble precursor which can be extracted from tissues in which collagen fibres are being laid down or removed. Furthermore, the formation of this precursor stops abruptly with starvation, scorbutus, or any other disturbance which halts growth.

The proceedings were by no means monopolized by the collagentsia. G. Asboe-Hansen and B. Sylvén discuss mast cells and their relation to heparin and other polysaccharides, and Karl Meyer gives a masterly exposition of the structure of the chondroitin sulphates. There is also new information about the protein component of the interfibrillary ground substance. According to A. Neuberger it is partly serum albumin derived from the circulating plasma, but Joan Bowes and Helen Muir both present evidence of other non-fibrous ground-substance proteins that must be reckoned with. Sylvia Fitton Jackson's electronmicrographs of transverse sections of tendon demonstrate this interfibrillary material and the lack of hexagonal close packing in a striking fashion. The nature of reticulin is admirably presented by A. H. T. Robb-Smith, and there are brisk discussions on elastin and its relation to and interconvertibility with collagen by D. A. Hall and S. M. Partridge, followed by I. Bango and J. Baló on elastases. Indeed,

there are so many important contributions that it is impossible to mention all of them; suffice it to say that for those who want authoritative, up-to-date information about connective tissue this book is a necessity.

J. H. KELLGREN.

HEREDO-RETINOPATHIA CONGENITALIS

Heredo-retinopathia Congenitalis: Monohybrida Recessiva Autosomalis. A Genetical-Statistical Study. By Carl Henry Alström in clinical collaboration with Olof Olson. (Pp. 178. No price.) Lund: *Hereditas*, vol. 43. 1957.

In a study on blind children in the one central elementary school for the blind in Sweden, the material covering the 50 years from 1897 to 1948, Alström and Olson have isolated a substantial group showing an affection with clear-cut features. The affection was responsible for some 10% of all blindness; it was hereditary, autosomal recessive in character, the proband material leading to 105 families, with 175 affected and 303 unaffected sibs. The blindness was produced by a fundus anomaly which was recorded under a variety of labels, such as "congenital amaurosis," "congenital optic atrophy," and "retino-choroiditis." Actually these lesions were different aspects of a progressive affection: early in infancy there were slight or no fundus changes, giving "congenital amaurosis"; later on the pigmentary reactions of the retino-choroiditis type dominated, and extended over a wide range of lesions from minute round pale spots at the periphery, scarcely visible, to heavy pigmentation scattered throughout the fundus. Whilst some optic atrophy and a moderate degree of narrowing of the vessels were common, optic nerve lesions were not as conspicuous as in cases of retinitis pigmentosa with equally severe impairment of sight. Associated conditions were cataract and keratoconus, cataract being present in some 10% among the youngest patients, and increasingly in the higher age groups; keratoconus was an exceptional finding in young patients, but the incidence again increased with age. Different members of the same sibship showed the different components to a variable degree; variations occurred not only with age, but as between families and between individuals within the same family.

This study helps considerably in clearing up some of the diagnostic difficulties met in blind infants. For one thing it disposes of "cortical blindness"—a frequent escape from a real difficulty; it also emphasizes the existence of a retinal lesion more severe than retinitis pigmentosa in that it is present at birth and produces blindness almost from the beginning. The polymorphism of the fundus lesion recalls an inflammatory reaction, and, as such, supplements the somewhat similar reactions recorded for generalized fundus dystrophy, a dominant genetic affection seen in middle age. The present study is rather fuller on its genetic than on its ophthalmoscopic aspects; it is particularly regrettable that there are no fundus illustrations to show the different stages of the affection, and it is to be hoped that this may be remedied in a more strictly ophthalmological study.

ARNOLD SORSBY.

FRENCH PRACTICE IN CHEST DISEASES

Techniques et Thérapeutiques en Pneumologie. New Series 1. Edited by Pierre Bourgeois and J. Turiaf. (Pp. 220. 1,400 frs.) Paris: Expansion Scientifique Française. 1957.

Techniques et Thérapeutiques en Pneumologie. New Series 2. Edited by Pierre Bourgeois and J. Turiaf. (Pp. 248; illustrated. 1,400 frs.) Paris: Expansion Scientifique Française. 1957.

These two paper-backed volumes contain a series of essays describing the techniques and therapeutic measures used in respiratory diseases at the Hôpital Bichat, Paris. The range of subjects covered by the 19 authors is wide, including both tuberculous and non-tuberculous diseases. Among the 34 chapters are contributions on such diverse matters as the technique of irradiation of bronchial carcinoma, tracheotomy in respiratory insufficiency, present views on B.C.G., and the lung in mitral stenosis. For the most part the chapters constitute individual essays on problems of daily interest in clinics dealing with respiratory disease, discussing them clearly and didactically in the light of recent advances in knowledge. Two of them have titles which, to our ears, have a rather old-fashioned ring; they deal with the present position of spa treatment in asthma ("Actualité du thermalisme dans l'asthme") and sulphurous spa treatment of bronchial suppurations ("Traitement thermal sulfureux des suppurations bronchiques"). The names of authorities are quoted throughout the text, and presumably are intended to refer to their published works; but in only one article, an excellent discussion of the problem of anterior cardiophrenic shadows, is there a bibliographical list of references. These two books provide a most useful indication of current French practice in diseases of the chest.

J. G. SCADDING.

HUMAN GENETICS

Proceedings of the First International Congress of Human Genetics, Copenhagen, August 1-6, 1956. Edited by Tage Kemp, Mogens Hauge, and Bent Harvald. In five parts. (Part I—pp. 1-316+xvi; Part II—pp. 317-502; Part III—pp. 503-613; Part IV—pp. 1-248; Part V—pp. 249-512; illustrated. No price.) Basle, New York: S. Karger. 1957.

The Congress on Human Genetics in Copenhagen in 1956 was the first such congress to be held, and the proceedings now published give an admirable panoramic view of the growing points of human genetics. The first volume is concerned with the estimation of mutation rates in man, with the effects of radiation on the mutation rate, and with heredity in cancer; the second with population genetics and physical anthropology; the third with blood groups in relation to anthropology, law, and medicine; the fourth and fifth with clinical genetics, including special sections on diseases of the nervous system, eyes, skin, teeth, and congenital malformations.

Most of the papers are in full; others are abstracts giving references to more complete accounts elsewhere. About the only major topic which is not discussed are the striking new advances that have been made in the chemical structures of deoxyribose nucleic acid and of the chromosomes. Few of the papers present really new material, and the findings given will mostly be familiar to those who read the American, English, Scandinavian, and French genetical periodicals, which cover the four areas where most work on human genetics is now being carried out. It is pleasant, however, to see work of good quality being reported from countries as far apart as Holland and Israel, Egypt and Chile. Unfortunately there are no authors from behind the Iron Curtain, perhaps because the prevailing ideology is so strongly environmentalist.

C. O. CARTER.

In *Purbeck Marble* (Hutchinson and Co. Ltd.; price 10s. 6d.) Dr. Llewellyn Pridham tells an exciting story for children about rival enterprises to supply the famous Dorset stone for the building of St. Paul's Cathedral. The young hero and heroine set out with courage and determination to win the contract from the great Sir Christopher Wren. The plot calls for trouble with a sinister villain named Grue, a sea battle with a French privateer, and a final race between two rival wagon teams. Dr. Pridham writes with authority and affection about his home county of Dorset, and this intimate touch gives the book a real sense of atmosphere which should make it acceptable to both older and younger children. More especially for the older ones the author has prefaced each chapter with apt quotations from John Masefield, while for the younger ones Grace Lodge has drawn some neat and lively illustrations, two more factors which add further colour to a sturdy and unusual tale.

The fourth edition of Dr. H. J. Parish's *Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment* (E. and S. Livingstone, Edinburgh, 1958; 30s.) has been considerably revised to incorporate the most recent advances in the subject. There are now five chapters on immunization against virus infections, including one on poliomyelitis vaccine.

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STEROIDS IN TREATMENT OF ASTHMA

During the last two years cortisone has been partly replaced in the treatment of asthma by the delta derivatives prednisone and prednisolone. The latter drugs are five times more potent than their predecessors and seven times more expensive, but they have the advantage of virtually no salt-retaining effects. All these compounds suppress the symptoms of allergic disease if used properly, often to an extraordinary extent. They are in no sense a cure. As well as obviously lessening the bronchospasm, they help in the improvement of the patient's general condition and morale and enable him to tackle his disease more successfully. There is yet little or no understanding of the mechanism by which these hormones produce their effects.[1 2]

They are not without danger.[3] Long-term treatment causes suprarenal atrophy, with the result that the patients are apt to die suddenly, or else have severe stress reactions if injured in an accident, if subjected to an operation or anaesthetic, or if an acute infection develops. Liability to infection is in any case increased, since steroids reduce the body's resistance; and this includes tuberculosis. No patient with any suspicion of active tuberculosis should be treated with steroids if it can be avoided, and it may be necessary to combine steroids with antituberculosis drugs. Particular care is also worth taking if steroid therapy has to be given to a diabetic. Other dangers are the development of peptic ulcers and a liability to their perforation and haemorrhage, osteoporosis, with occasional development of fractures, and acute psychotic states, especially in those patients who have a history of mental illness.[4] R. A. Kern[4] has published interesting mortality statistics from the United States, where the total death rate has steadily fallen since 1939. The death rate of patients with chronic or rheumatoid arthritis remains level. But deaths from asthma suddenly increased in 1951 by nearly one-half, and this increase has been maintained. This is the period when steroid therapy has been in vogue. The rise is mainly confined to patients between 50 and 79 years of age. There is no proof that steroid therapy is the cause of the sudden rise, but the figures are alarming. Steroids were not released for general use in Great Britain until 1956; the Registrar-General's published statistics have not yet reached this period, and they will be awaited with interest.

Steroid therapy is undoubtedly a most valuable method of treatment for severe chronic asthma and status asthmaticus. Moreover, in the elderly chronic bronchitic when bronchial obstruction is severe and not responding to antibiotics and antispasmodics, its early administration while continuing the antibiotics is often helpful. It reduces hospital stay and saves beds at a time when they are precious in areas where chronic bronchitis is endemic, and these steroids do not affect the suprarenal glands adversely, provided they are used on a short-term basis.[1 2]

Steroids are readily prescribed and administered in general practice, but they are best reserved for those cases in which full treatment without them has failed, and a consultant opinion is normally worth obtaining before beginning them, especially in the case of children. They should be given in short courses starting with a large dose and lessening it daily. A good scheme is to start with 300 mg. of cortisone on the first day in the form of twelve 25-mg. tablets, and reduce the dose by one tablet daily. The course will thus last twelve days. Prednisone and prednisolone are given in one-fifth of the dosage, and as the tablets are 5 mg. each the same number are used. The importance of this procedure is to protect the suprarenal glands from damage. The course can be repeated in two or three months.[1 2] Some physicians believe that if long-term oral treatment has to be carried out it is advisable to give in addition periodic injections of A.C.T.H.-gel to stimulate the glands and prevent atrophy.[2] There is an advantage in giving cortisone rather than the newer steroids apart from the economy. The newer steroids are more potent and in equivalent doses have the same side-effects except that the warning of rapid gain in weight and oedema does not occur. Consequently there is a greater risk of danger, especially when large doses are used. They also cause suprarenal atrophy.[4] In spite of the dangers of steroid therapy in cases of asthma, especially when given in small doses over a long period, manufacturers are selling individual combinations of steroids with aspirin, antihistamines, antispasmodics, and aluminium hydroxide.[4] It is safer to use the drugs separately, each in the appropriate dose for the patient under treatment. In short, steroids have made a great difference to the treatment of severe chronic asthma, but they have their dangers.

[1] Brockbank, W., Savidge, R. S., and Brebner, H., *Lancet*, 1957, **2**, 666.
[2] Unger, L., and Johnson, J. H., *Ann. Allergy*, 1957, **15**, 563.
[3] *Brit. med. J.*, 1955, **1**, 216.
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IRON STORES AND IRON DEFICIENCY

Ionic iron is so essential and yet potentially so toxic that all living matter has evolved means of storing and transporting it in safely chelated forms. In human and animal tissues iron is bound to a specific protein to form a water-soluble chelate, ferritin. Larger, water-insoluble aggregates are present as haemosiderin, which, together with ferritin, constitute the principal stores of iron. For transport purposes, iron circulates in the plasma bound to a β_1 globulin, transferrin. While most of the iron is ferric, it seems that only the ferrous form can be transferred across cell membranes. Anaerobiosis *in vitro* or hypoxia *in vivo* permits the release of iron from ferritin by reducing disulphide bridges to free sulphydryl groups.[1] An interesting connexion of hypoxia with xanthine oxidase has been suggested, linking the release of iron with purine metabolism and uric acid formation.[2]

Our views on the nature of the iron stores are changing rapidly. From being considered a geological deposit in the tissues, haemosiderin is now rehabilitated as a readily available source of iron.[3] Under the electron microscope it is seen to consist of granules resembling ferritin, embedded in a matrix which histochemically is found to contain mucopolysaccharide, protein, and lipid, and it is suggested that haemosiderin is derived from altered mitochondria or "siderosomes."[4] The idea still persists that excessive deposits of haemosiderin can induce haemochromatosis, but there is now strong evidence to the contrary.[5-7] In fact the only effects of such excessive accumulation of iron appear to be attributable to a relative deficit of tissue antioxidants, principally vitamin E.[8]

In the human foetus iron reserves largely take the form of an excess mass of haemoglobin, which develops only in the last trimester. The premature infant is thus born with short supplies of iron; even for the full-term child Nature's provision of iron can hardly be considered bountiful for the rapid growth of the first year. Sceptics who doubt whether maternal anaemia requires treatment may be interested to note the results of R. C. Sisson and C. J. Lund,[9] who found that the infants of anaemic mothers frequently share the iron deficiency. In these infants the haemoglobin mass was on the average 15% below, and the red cell volume 12.5% below, the figures for a control group of babies born of non-anaemic mothers; the serum iron level was 30% lower.

Iron depletion develops in a manner reminiscent of many vitamin deficiency states: that is, there is often a long-drawn-out stage of latent or subclinical deficiency which has hitherto remained largely unrecognized. Such a state is characterized by great diminution of the body's stored iron before the peripheral blood, and particularly the haemoglobin level, have revealed any striking change.[10 11] Recent work on the amount of cytochrome c in liver and kidneys of rats on an iron-deficient diet has shown that the level of this respiratory enzyme falls before anaemia becomes notable.[12] Decreased levels of liver and kidney catalase, another iron-containing enzyme, have previously been reported in iron-deficiency anaemia. Thus these enzymes may not have priority for the available iron as had been believed. Much remains to be done before the vague symptomatology of subclinical iron deficiency can be clearly related to changes in the iron-containing tissue-enzyme systems of the body. But the idea that these enzymes suffer loss as part of the general depletion of iron stores which precedes frank anaemia, and are reconstituted by therapy designed to fill the iron stores, is worthy of further investigation.

The degenerative changes in epithelial tissues of anaemic patients described by D. R. Paterson[13] and A. Brown Kelly[14] have now been recognized in the absence of overt anaemia. Nevertheless, the epithelial changes respond to iron therapy. Dyspepsia and loss of appetite is a common complaint of patients with iron deficiency. Although achlorhydria in the past was incriminated as a cause of iron deficiency, it would now seem that hypochlorhydria and even histamine-fast achlorhydria can develop as a consequence of this condition[15]; the gastric mucosal changes respond specifically to iron therapy in early

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[8] —— and Smith, J. P., *Brit. J. exp. Path.*, 1958, **39**, 59.
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[13] Paterson, D. R., *J. Laryng.*, 1919, **34**, 289.
[14] Kelly, A. B., ibid., 1919, **34**, 285.
[15] Witts, L. J., *Anaemia and the Alimentary Tract*, Royal College of Physicians of Edinburgh, 1956, Publication No. 7.
[16] Leonard, B. J., *Lancet*, 1954, **1**, 899.
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[18] Slack, H. G. B., and Wilkinson, J. F., *Lancet*, 1949, **1**, 11.
[19] Jennison, R. F., and Ellis, H. R., ibid., 1954, **2**, 1245.
[20] Hutchison, H. E., *Blood*, 1953, **8**, 236.
[21] Davidson, W. M., and Jennison, R. F., *J. clin. Path.*, 1952, **5**, 281.
[22] Beutler, E., Drennan, W., and Block, M., *J. Lab. clin. Med.*, 1954, **43**, 427.
[23] Kerr, L. M. H., *Biochem. J.*, 1957, **67**, 627.
[24] Bothwell, T. H., Pirzio-Biroli, G., and Finch, C. A., *J. Lab. clin. Med.*, 1958, **51**, 24.
[25] Pirzio-Biroli, G., Bothwell, T. H., and Finch, C. A., ibid., 1958, **51**, 37.
[26] Bothwell, T. H., and Finch, C. A., *Amer. J. dig. Dis.*, 1957, **2**, 145.
[27] Finch, S., Haskins, D., and Finch, C. A., *J. clin. Invest.*, 1950, **29**, 1078.
[28] O'Sullivan, D. J., Higgins, P. G., and Wilkinson, J. F., *Lancet*, 1955, **2**, 482.

cases,[16] whereas achlorhydria does not itself influence iron absorption.[17] Dramatic improvement in the subjective symptoms of iron deficiency sometimes occurs soon after beginning effective therapy and before correction of the anaemia.[18 19] These observations are like those made in cases of pernicious anaemia, when patients express a feeling of well-being within a few days of vitamin B_{12} injection.

There are no simple means of assessing the condition of the iron stores. Tests based on the serum-iron response following an orally administered dose of iron have been shown to be fallacious; and radio-isotope techniques have not solved the problem. For objective evidence the only adequate measure is the examination of a satisfactory specimen of bone marrow, either microscopically for haemosiderin[20–22] or chemically for total non-haem iron.[23]

Since repletion of iron stores is of such fundamental importance, how may it best be achieved? The absorption of iron from dietary sources or orally administered iron salts has been the subject of considerable investigation, and it seems clear that something more than a "mucosal barrier" must be postulated to explain the facts. A major influence is exerted by the activity of the erythroid marrow and by the iron content of the body. The connexion between marrow and intestinal mucosa is not through plasma-iron or haemoglobin levels, so that anaemia in itself does not regulate iron absorption.[24–26]

The significance of quantitative studies of iron uptake must be judged in relation to the techniques used and the doses of iron given. Thus at a dose of 4–5 mg. iron salts were absorbed to the extent of 15% in normal subjects and 80% in cases of iron deficiency. But over the clinical dose range of 2–6 mg. of iron per kg. body weight the normal subject absorbs a variable proportion, usually 2–4%; this figure rises to 20% in iron deficiency. Neither ascorbic acid nor cobalt exercises a significant influence, though the presence of food reduces the absorption of iron by approximately one-half: so that under the ordinary circumstances of clinical treatment the absorption of iron salts may not exceed 10% even in severe iron deficiency.[24 25] Once the anaemia of iron deficiency has been corrected and erythropoietic activity has returned to a basal level, absorption of iron returns to normal levels despite continued depletion of the iron stores. Hence it seems likely that little replenishment of reduced iron stores can be brought about by iron entering through the intestinal mucosa, except by very prolonged treatment.[22 27] In this, as in other respects,[28] various ferrous salts display no significant differences. The only rapidly effective method at present available for replenishing the iron stores is by the parenteral route.

MONKEYS FOR POLIOMYELITIS VACCINE

Monkeys are needed for both the production and the testing of the Salk type of vaccine, and about eight are required to produce enough vaccine to immunize 2,500 children. Since Great Britain has a population of about 800,000 children at each year of age, a large number of monkeys are required for the immunization programme. Two types of monkey are used. The main one is the rhesus monkey; nearly all of them come from India, but a few from East Pakistan. The other is the cynomolgus monkey, a smaller and less robust species which comes from Indonesia and the Philippines. The monkey population of India has been estimated to be about the same as the human population—that is, approaching 400 million. Many are to be found in the neighbourhood of villages and towns, where they damage crops and even houses, and readily acquire tuberculosis from man. Others inhabit jungle areas where tuberculosis is almost unknown. All are liable to suffer from various types of dysentery and a number of virus diseases. They tend to live in groups that may be a few hundred strong, and they have a fairly well organized social pattern. In some parts of India the Hindus regard them as sacred animals and there is serious objection on religious grounds to killing them. These objections are not found in Moslem communities.

The monkeys are trapped by professional trappers who follow the colonies around the country, often to places difficult of access. The most popular methods of trapping the monkeys are baited spring nets and funnel-shaped traps. Some of the animals trapped will have to be destroyed or released because they are unfit for export. When caught, the monkeys are transferred to the base in bamboo cages, and the journey by bullock cart, train, and lorry may last several days. At the base they are sorted into groups of approximately equal size or age and put into larger cages holding 50 or 100. They are fed and, in many cases, treated prophylactically for dysentery and other diseases. They may be tuberculin-tested. Some 10% of those arriving at the base are unfit for shipping on account of age, injury, or sickness. When many hundreds have been collected at the base, they are placed in travelling cages and loaded on to animal freighter aircraft. The travelling cage in normal use is of a pattern that has been shown by experience to preserve the monkeys in the best possible health during their air journey to the importing country. From 800 to 1,600 monkeys may go in a single plane load. The planes are heated, ventilated, and now nearly always pressurized, and one or two monkey-attendants travel with them. The monkeys are fed and watered on the journey, and at stops for refuelling are usually removed from the planes and their cages cleaned out. Airlines of importing countries have paid attention to providing the best possible conditions for transport and reception, and a load of healthy monkeys will tolerate a journey of many days, with little or no loss in transit. Indeed, the monkeys' health may improve on the journey owing to their receiving better food than in the wild state. So long ago as August, 1955, the Medical Research Council produced recommendations for the humane shipment of

monkeys which were considered to be acceptable and satisfactory. The worst of the monkeys' hardships occur before they reach the plane, and this is a matter for the exporting countries to control.

The export of monkeys in such numbers is big business, and only the large collector can afford to charter special planes or to make use regularly of normal freight services. Moreover, only large operators can guarantee to supply monkeys in the numbers in which they are required. For this reason the supply of monkeys is in the hands of a few suppliers who have very extensive financial backing, and to whom most of the trappers are well known. Owing to the necessity for such a large and complicated organization for the collecting, concentration, and shipment of monkeys, we can expect to get them only from those countries where such an organization exists. East Pakistan has so far not been providing regular shipments of large numbers. An additional difficulty there is the scarcity of suitable food for the monkeys. It would be an advantage, however, for us to obtain regular shipments of monkeys from East Pakistan, for the supply might be less liable to interruption from political or religious motives.

The supply of cynomolgus monkeys from Indonesia and the Philippines is plentiful and becoming well organized. But this species is more delicate, and the longer haul makes the freightage higher. Moreover, they may cost dollars instead of sterling. It might in time be possible to obtain large numbers of monkeys from West, Central, and East Africa. The African species are different, but probably would serve well enough for the purpose of vaccine production, though more experience with them is needed to confirm this. Their collection in most parts of Africa is not yet properly organized, nor are there such good air services for transport, but there is little doubt that these difficulties could be overcome.

While the production of poliomyelitis vaccine is dependent on the supply of monkeys, and as more and more countries introduce mass vaccination, the number of monkeys required will continue to grow. Indeed, India herself can expect to have a poliomyelitis problem within the next ten years as the general standard of hygiene in the country improves, because the incidence of poliomyelitis tends to increase with the raising of the standard of general hygiene. Such countries therefore will rely on the West for the development of vaccines as much as the West does on them for the supply of monkeys. Clearly an urgent necessity is the devising of technical methods that will obviate the use of these expensive and delicate animals.

THORACOPLASTY FOR PULMONARY TUBERCULOSIS

Of the methods of collapse therapy used in cases of pulmonary tuberculosis, paravertebral thoracoplasty proved the safest and most effective. The operation became standardized after a long period of development. E. de Cérenville,[1] of Lausanne, first had the enterprise to remove parts of several ribs for the treatment of tuberculous cavities in the lung in 1885; previously he had used the method for chronic empyema. Swiss and German surgeons improved the operation by paravertebral section of the ribs, removing more and larger portions; but, while increasing the effectiveness of the collapse, they increased its risks. Treatment was made safer by a more restricted attack on the upper part of the lung. J. Alexander,[2] of Michigan, emphasized the need for removing adequate portions of the ribs over the cavity, including the first, and performing the operation in several stages. This made the operation more tolerable, and more effective in collapsing those segments of lung most involved. It avoided the removal of ribs from the lower thorax and actually lessened the risk of aspiration into the lower lobe. Results were improved and mortality much diminished. C. Semb's operation of apicolysis[3] further improved collapse by freeing the apex and the endothoracic fascia from the parietes.

Before chemotherapy for tuberculosis became universally available, a number of surgeons had successfully treated cases by staged paravertebral thoracoplasty with extrapleural pneumolysis. Holmes Sellors and his colleagues[4] have recently published the results of a consecutive series of 231 patients, so adding to the few previous British reports. Their patients were operated upon in the two years before December, 1949, and the follow-up covers six to eight years. The series is representative of patients generally thought suitable for this treatment, equally divided between the sexes, and nearly all in the age range 20–50 years. Bilateral disease was present in 58%; 48% had cavities of 1½ in. (4 cm.) diameter and 84% had involvement of two zones or more. All but six had at some time yielded sputum containing tubercle bacilli, though six weeks before the operation nearly a quarter had become sputum negative. None had significant chemotherapy. Only three patients died as a result of the operation, two of these having far-advanced disease. By the end of the follow-up period the total deaths were 14%, but 96% of the survivors were fit for work. The mortality was considerably influenced by the inclusion of advanced cases, since nearly a third of those with four or more zones of infection died. Clearly these had active disease in the opposite lung which could hardly be influenced directly by the operation; indeed, lower-zone disease in the same side is also an unfavourable factor. As with other series —for example, that of R. Douglass and E. B. Bosworth[5] —if the disease was rendered quiescent the risk of relapse was low, and later deaths occurred principally in those patients with still active disease.

Evidently this operation was highly successful in the hands of an experienced team. What is its place to-day? Pulmonary resection for tuberculous disease seems paramount, and collapse methods such as extrapleural and intrapleural pneumothorax are in the discard. But just as resection appeared to have ousted thoracoplasty, so now resection has been rendered unnecessary by

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[2] Alexander, J., *The Collapse Therapy of Pulmonary Tuberculosis*, London, 1937.
[3] Semb, C., *Acta chir. scand.*, 1935 (*Suppl.* 37), **76**, 1.
[4] Gough, J. H., Barlow, D., Holmes Sellors, T., and Thompson, V. C., *Thorax*, 1957, **12**, 241.
[5] Douglass, R., and Bosworth, E. B., *Amer. Rev. Tuberc.*, 1954, **69**, 930.
[6] Holst, J., *Nord. Med.*, 1952, **48**, 1288.
[7] Fox, W., Wiener, A., Mitchison, D. A., Selkon, J. B., and Sutherland, I., *Tubercle*, 1957, **38**, 71.

adequate prolonged chemotherapy in many patients in whom it would previously have been attempted. Thoracoplasty and resection are not necessarily alternative or rival methods, and even when surgery is essential chemotherapy now limits the extent of operative treatment. Modifications of the standard paravertebral thoracoplasty by J. Holst[6] and by others have improved the operation and lessened deformity. Modified thoracoplasties are commonly done after lobectomy and some other resections.

Thoracoplasty has some obvious drawbacks—the deformity, the disordered muscle balance, impairing respiratory function, and the retention of a lung with damaged bronchi which are a potential site for chronic infection. Not a few of the late deaths are due to cor pulmonale. Certainly the number of primary paravertebral thoracoplasties required to-day is drastically fewer than ten years ago. Yet there probably remains a place for the standard operation. Resection is not always possible even when desirable. The resistant micro-organism becomes an increasing threat: about 5% of newly diagnosed cases show evidence of resistance to at least one standard drug.[7] If this trouble increases, thoracoplasty may yet be more often required, for excisional surgery is dangerous without effective cover by drugs.

GENES AND AMINO-ACIDS

Recent work by V. M. Ingram, of the Medical Research Council Unit attached to the Cavendish Laboratory, Cambridge, has been of outstanding importance in elucidating genetic processes, and his chemical analysis of haemoglobins A, S, and C[1–3] represents a most important development in the field of haemoglobinopathies. The globin part of the haemoglobin molecule contains some 600 amino-acids. As globin is made up of two identical mirror-image halves Ingram could confine himself to the chemical identification of 300 amino-acids. These 300 amino-acids, known to be of nineteen different kinds, are arranged in two chains of about 150 each. Trypsin hydrolyses an amino-acid chain only at points where lysine or arginine occurs, and in each half-molecule of globin there are about 26 of these two amino-acids placed at intervals in the two chains. By tryptic digestion Ingram was therefore able to break down the two chains of the half-molecule into 28 fragments, each of them a peptide chain containing about one dozen amino-acids. By a combination of electrophoresis and chromatography these 28 peptides could be separated and identified. Ingram found then that the difference between haemoglobins A, S, and C could be narrowed down to one particular peptide containing nine amino-acids. Eight of these were the same in all three, but one was different: glutamic acid in haemoglobin A, valine in haemoglobin S, and lysine in haemoglobin C.

The three haemoglobins are the products of allelic genes.[4] The formation of haemoglobin S or C instead of normal adult haemoglobin A is apparently the result of gene action on this one small part of the haemoglobin molecule. The inheritance of haemoglobins and other characters is carried from generation to generation in the chromosomes, which form the nuclei of the germ cells. These chromosomes are chains of nucleic acids, and the genes are thought to be individual nucleic acids in the chains. As such they are self-reproducing and either directly or indirectly they determine the structure of particular proteins. The mutation from the haemoglobin A gene to its alleles responsible for haemoglobins S or C must then be a minute change in one of these nucleic acids. It is clear that Ingram's work is of great importance beyond the subject of the synthesis of the haemoglobin variants with which it is immediately concerned. Two problems of particular urgency on which it has a direct bearing are the development of cancerous change and the effect of radiation on the human mutation rate.

[1] Ingram, V. M., *Nature (Lond.)*, 1956, **178**, 792.
[2] —— ibid., 1957, **180**, 326.
[3] Hunt, J. A., and Ingram, V. M., ibid., 1958, **181**, 1062.
[4] Ranney, H. M., *J. clin. Invest.*, 1954, **33**, 1634.

ANTIBODY PRODUCTION IN HEPATIC CIRRHOSIS

Though active immunization against tetanus by injection with toxoid has been customary in the armed Forces for some years, among the general population it is practised only to a small extent. The great majority of the civilian population is therefore unprotected, and the use of prophylactic inoculation with antitoxin in possible cases of exposure is likely to remain the standard practice for many years. The administration of the relatively large amounts of heterologous serum which this entails is itself not without risk, and even fatal reactions have occurred. A further objection springs from the occasional failure, albeit rare, of such heterologous sera to protect owing to the presence of antibodies to them engendered by a previous prophylactic injection.[1] Attempts have therefore been made to produce hyper-immunization in human beings so that their gamma globulin could replace the horse sera now in common use.[2] Unfortunately, a level of at least 100 units of antitoxin per ml. is necessary to make the production of adequate gamma globulin a practicable proposition, and such levels are rarely attained in normal subjects. However, some years ago W. P. Havens and colleagues[3] observed that some Schick-negative patients with hepatic disease give an exaggerated antibody response to diphtheria toxoid. The possible use of similar patients for the production of tetanus antitoxin, therefore, seemed worth studying.

These investigators selected twenty-eight veterans of the second world war suffering from hepatic cirrhosis associated with chronic alcoholism, and determined in them the level of circulating tetanus antitoxin before, and at intervals after, the injection of a booster dose

[1] Littlewood, A. H. M., Mant, A. K., and Wright, G. P., *Brit. med. J.*, 1954, **2**, 444.
[2] Havens, W. P., Jr., Myerson, R. M., and Klatchko, J., *New Engl. J. Med.*, 1957, **257**, 637.
[3] —— Shaffer, J. M., and Hopke, C. J., *J. Immunol.*, 1951, **67**, 347.
[4] Popper, H., and Schaffner, F., *Liver: Structure and unction*, 1957, New York and London.
[5] Sabin, F. R., *J. exp. Med.*, 1939, **70**, 67.
[6] Coons, A. H., and Kaplan, M. H., ibid., 1950, **91**, 1.
[7] Oakley, C. L., Warrack, G. H., and Batty, I., *J. Path. Bact.*, 1954, **67**, 485.
[8] Coons, A. H., Leduc, E. H., and Connolly, J. M., *J. exp. Med.*, 1955, **102**, 49.
[9] Harris, S., and Harris, T. N., *Amer. J. Med.*, 1956, **20**, 114.

of tetanus toxoid. All had been actively immunized some ten years previously. No parallel series of normal subjects was studied, since the response of normal subjects has been thoroughly established by several other investigators. The results obtained by Havens and his colleagues largely confirmed the previous results with diphtheria toxoid in that five of the twenty-five individuals that were adequately investigated were hyper-reactors, with a peak level of antitoxin exceeding 100 units per ml., and in one individual reaching 915 units per ml. Correlation of the response with various clinical features was not clearly established, but, in general, patients in a poor state of health with splenomegaly and ascites responded badly, while the best reactors had neither ascites nor splenomegaly and their general health was classified as fair or good.

It seems, therefore, that it should be possible to select from patients with cirrhosis a group of volunteers who could act as a source of immune gamma globulin for tetanus prophylaxis. Much more, however, will need to be known of the possible adverse effects of the necessary immunization process upon such individuals. The impairment of albumin synthesis by the cirrhotic liver is also a serious drawback, since the repeated phlebotomies required would entail repeated injections of albumin to reduce the strain on the synthesis of hepatic albumin. It is unlikely, therefore, that cirrhotic subjects could ever be used as a source of tetanus antitoxin on a commercial scale. But the findings of Havens and his collaborators are of theoretical interest in relation to antibody synthesis. The raised serum gamma globulin so characteristic of patients with chronic liver disease may well be a more general expression of their heightened ability to respond to antigenic stimuli. The presence of hepatic enlargement and the absence of splenomegaly in those patients who responded best to a booster dose of toxoid would seem to exclude the spleen as the organ responsible and to emphasize the role of the liver itself in the production of antibody. The hypertrophy and basophilia of the Kupffer cells correlate fairly well with the increased serum gamma globulin,[4] and the role of these cells in formation of antibody has received strong support in experiments with azo dyes[5] as well as by the more recently introduced fluorescent-antibody technique.[6] Experimental evidence acquired in the last 20 years,[7–9] however, has shown that the ability to form antibodies is widely distributed throughout the lymphoreticular tissues of the body, and a hyper-reaction of the whole of this system may well underlie the results of Havens and his colleagues.

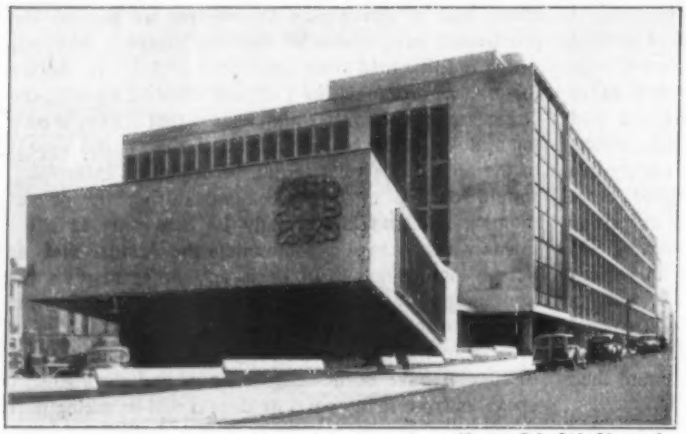
ANNUAL CLINICAL MEETING AT SOUTHAMPTON

Last November the Council of the B.M.A. approved the proposal of the Organization Committee that a second scientific meeting of the Association should be held each year. This will be called the Annual Clinical Meeting of the B.M.A. Southampton's invitation to hold the first of these meetings in that town was gratefully accepted, arrangements went ahead with commendable speed, and in this week's *Supplement* we publish the provisional programme of the Southampton Meeting, which is to be held from December 4 to 7. In putting forward its proposals for a second scientific meeting the Organization Committee emphasized that it should be a scientific function of high standard that would appeal to the postgraduate: it should be organized informally, should occupy a long week-end during the winter months, and should normally be held only in those towns which cannot accommodate the Annual Meeting of the Association. In these and other respects the Southampton Meeting looks like being a model of what the Organization Committee had in mind. As can be seen from the provisional programme, the subjects for discussion have been wisely chosen, and distinguished speakers from many parts of Britain will be taking part. A remarkable new feature will, it is hoped, be introduced in the form of a transatlantic clinical conference, during which Southampton will be linked by radiotelephone with Minneapolis, where the American Medical Association will be holding its winter clinical meeting. On the social side there will be a reception by the Mayor of Southampton, an informal dinner, and various diversions arranged by the Southampton Division. The local officers at Southampton, under the chairmanship of Dr. R. S. Russell-Smith, have enthusiastically undertaken the considerable burden of arranging this meeting, and it is to be hoped many members will support their efforts by visiting Southampton for what promises to be an instructive and enjoyable week-end.

THE SECRETARYSHIP OF THE B.M.A.

Dr. Angus Macrae retires under the age limit from the office of Secretary of the B.M.A. in November of this year. He succeeded Dr. Charles Hill in 1950. His kindliness and quiet courtesy have endeared him to the many who have come into contact with him on official and unofficial occasions. Under his Secretaryship the business of the Association has been conducted with punctiliousness and exactitude. Dr. D. P. Stevenson was elected as his successor by the Council at its meeting last week. Dr. Stevenson joined the staff in 1946 as Assistant Secretary, and was appointed Deputy Secretary in 1948. Most of his professional life was spent in the Army, and from 1942 to 1946 he was Assistant Director General, Army Medical Services. He has acted as secretary to many important Association committees, and notably the General Medical Services Committee, being closely associated with Dr. S. Wand (then chairman of that Committee) in the negotiations leading up to the Danckwerts award. At the age of 47 he will bring to the important office of Secretary of the Association energy, capacity for hard work, an equable temperament, and a great loyalty to the causes he is serving.

The next session of the General Medical Council will open on Tuesday, June 3, at 2.15 p.m., when the President, Sir David Campbell, will take the chair and deliver an address.



[Stewart Bale, Ltd., Liverpool

The Pembroke Place aspect of the new building for the Liverpool School of Medicine. In the foreground is the flying lecture theatre.

LIVERPOOL SCHOOL OF MEDICINE

NEW BUILDING OPENED

On May 7 QUEEN ELIZABETH THE QUEEN MOTHER opened the new building for Liverpool University's School of Medicine. The picture shows its appearance from the Pembroke Place end, with the remarkable flying lecture theatre in the foreground. The building, which is the first stage in the school's reconstruction, was designed by Mr. A. G. BULLEN, F.R.I.B.A. It brings together under one roof the departments of pathology, bacteriology, pharmacology and general therapeutics, medicine, obstetrics and gynaecology; the subdepartment of radiodiagnosis; and the offices of the dean of the Faculty (Mr. J. M. Leggate). Hitherto all these departments have been widely separated and variously housed, one in a former nurses' home, one in a converted house, and another as the tenant of part of the city laboratories; only two have been in buildings erected for academic purposes—the department of pathology in the Thompson-Yates Laboratories built in 1898, and the department of obstetrics and gynaecology in the original building of the Royal Infirmary School of Medicine dating from 1844. Ultimately it is hoped to link the present building with a further block fronting Elizabeth Street so that the School of Medicine when completed will accommodate all the departments of the Faculty. At the moment the School has 506 undergraduate and 177 postgraduate students.

The framework of the building is reinforced concrete with pre-stressed concrete beams, and the Pembroke Place elevation, where the building abuts on the boundary of the University precinct, is faced with Portland stone. Inside, each department is on a separate floor, except for the department of pathology, which occupies two, and the teaching and research facilities for each department are in separate sections. There is also a separate animal wing to which departments have access, each at its own level. The main lecture theatre seats 250 people. Two smaller theatres hold 120 and 30 students respectively, and there are two practical classrooms with room for 100 students in each. In addition there is museum accommodation for the departments of pathology and obstetrics and gynaecology, staff accommodation, offices, etc. The building is air-conditioned throughout.

Opening Ceremony

The proceedings were opened by the Chancellor of the University, the MARQUESS OF SALISBURY. Before inviting the QUEEN MOTHER to declare the School of Medicine open, the Chancellor called upon Lord COHEN OF BIRKENHEAD to deliver an address.

One hundred and thirty years ago, said Lord COHEN, a Liverpool paper, the *Kaleidoscope*, had urged the establishment of a medical school. Only thus, it claimed, could be satisfactorily refuted "the erroneous and popular opinion—'that there is a great want of clever medical men in Liverpool'—so universal in London, and current everywhere." Only then should they "cease to be inundated with such shoals of Welshmen, Irishmen, and last and worse of all, Scotchmen." The exhortation was effective. In 1834 the Liverpool Royal Institution School of Medicine was established. Ten years later it was transferred to the Liverpool Royal Infirmary, where in 1844 was erected the Medical School and which until a few months ago housed one of the departments now occupying the new building. Since then the School's evolution had followed the pattern of all provincial medical schools. With advancing knowledge from the application to medicine of the basic sciences, and the immense development in the newer sciences of pathology and bacteriology, had come the demand for more accommodation, and with this the need for higher educational facilities in other fields. Thus their medical school had sown the seeds of Liverpool's University College, which was opened in 1882 and had blossomed into full university status in 1903.

Sixty years had passed since their University had witnessed a ceremony with to-day's purpose—when Lord Lister opened its Thompson-Yates Laboratories and received an honorary degree. History might not repeat itself, but historical situations recurred, and with them came the opportunity for reflection. At Liverpool they might well have lagged behind other schools in the comfort and modernity of their buildings, but the pride of any school lay not simply in the beauty and dignity of its architecture but in the contribution which those who laboured within its walls made to the advancement of learning and the ennoblement of life. It was not the intoxication of this memorable occasion nor a narrow parochial pride, said Lord Cohen, which led him to claim that by this standard Liverpool took second place to none. At Liverpool had been conceived and developed some of the most productive and creative ideas of the human mind. By a curious coincidence it was possible to vindicate that claim by referring briefly to three who, had they lived, would each in the past year have been a hundred years old—Sir Ronald Ross, Sir Robert Jones, and Sir Charles Sherrington. Ronald Ross was scientist, poet, mathematician, novelist, water-colour artist, and musician. His niche in the Valhalla of medical immortality was secure for his demonstration in 1898 of the mode of transmission of malaria by the mosquito. Since Ross's day, and following his example, the School had continued by its researches to unmask the means whereby literally hundreds of thousands of lives had been saved in tropical countries. Robert Jones was the founder of modern orthopaedic surgery, and his disciples were to be found throughout the world. The last of the triumvirate was Sir Charles Sherrington, who during his tenure of the George Holt chair of physiology from 1895 to 1913 was to make those contributions to our understanding of the workings of the nervous system which were to earn for him the epitaph—the greatest physiologist since Harvey. "These three men," said Lord Cohen, "in their lives and works typify the spirit which permeates this School and exemplify its history, for, as Emerson has wisely held, there is properly no history, only biography."

QUEEN ELIZABETH THE QUEEN MOTHER then declared the new building open.

Dr. Charles Berman, of South Africa, delivered the 13th annual James Ewing memorial lecture at the New York Academy of Medicine on May 1. His subject was "Primary Carcinoma of the Liver."

JOINT MEETING OF BRITISH AND DUTCH RHEUMATOLOGISTS

HEBERDEN SOCIETY IN LEYDEN

The Heberden Round and a joint meeting of the Heberden Society and the Dutch Society of Rheumatologists were held at Leyden on April 25 and 26. Besides the clinical and scientific discussions there was a most enjoyable social programme. The Burgomaster of Leyden gave a reception in the historic Lakenhal, and a dinner was held under the auspices of the International Study Centre for Rheumatic Diseases, Amsterdam.

Heberden Round

Professor J. GOSLINGS gave the annual Heberden Round at the University Hospital, Leyden. His theme was the association of pericarditis and rheumatoid arthritis. Thirteen cases were presented, three of which had come to necropsy. Most of the patients had severe, active rheumatoid arthritis, and some had other visceral involvement. Several showed the lupus erythematosus cell phenomenon. In four patients, however, pericarditis had been recognized where the duration of rheumatoid disease had been less than eighteen months. The clinical recognition of pericarditis might be difficult, as physical signs might be transient and the E.C.G. negative in cases showing pericarditis at necropsy. Professor Goslings thought that the difficulty of detecting pericarditis during life might explain some of the differences between its reported prevalence in patients with rheumatoid arthritis and in necropsy series.

Joint Meeting

Drs. S. A. DEN OUDSTEN and B. SPEYER (Rotterdam) had compared the frequency of spontaneous fractures of long bones and crush fractures of the spine in a group of adults with severe rheumatoid arthritis with that in a control group of comparable non-rheumatoid invalids. In both groups the age of the patient and the degree of immobilization contributed significantly to the development of both types of fractures, but there was no significant difference between the rheumatoid group and the controls. Furthermore, administration of cortisone in the usual therapeutic doses did not seem to enhance the incidence of fractures.

Drs. W. HIJMANS and H. R. E. SCHUIT (Leyden) discussed the lupus erythematosus (L.E.) cell phenomenon. In 2,000 patients with various diseases they had discovered 200 positive cases, but only one of these positive cases could not be classified as belonging to the group of so-called collagen diseases. The hypothesis (as yet unproved) that the L.E. cell is the result of an immunological mechanism had received strong support from many authors. It seemed that nuclear protein, or a part thereof, but not desoxyribonucleic, could be regarded as antigen, and the L.E. cell factor (a component of L.E. globulin) as auto-antibody. They had shown that the L.E. cell factor could react with the nuclei of calf thymocytes and of hen red cells. Even if phagocytosis were prevented, the typical "inclusion" bodies could be formed, although of course they were then free and unincluded, and therefore phagocytosis itself was not an essential part of the reaction. They had studied the proportions of hen red cells and human L.E. serum which would give the maximum number of L.E. cells. They had also shown that leucocytes would engulf nucleoprotein itself in the presence of L.E. factor, and discussed the possible significance of the L.E. phenomenon in the pathogenesis of the collagen diseases.

Dr. E. KRUYFF (Wassenaar) reported that, of 1,996 Dutch patients with ankylosing spondylitis treated by radiotherapy, in whom a follow-up rate of over 90% had been achieved, there had been 256 deaths, 25 of which were due to leukaemia or aplastic anaemia, thus confirming the enhanced incidence of leukaemia after radiotherapy, to which Van Swaay had called attention in 1950. These figures were compared with those obtained for England and Wales by the Medical Research Council. The statistics, however, were not strictly comparable because of differences in dosage, age, and completeness of follow-up (46% in the M.R.C. series). Several instances of leukaemia in patients treated with deep x rays for conditions other than ankylosing spondylitis were also reported. The incidence of leukaemia was steadily rising in the Dutch population as a whole.

Dr. L. STUBBE (Leyden) had found occult blood, as judged by a positive benzidine reaction, in the stools of about 70% of 180 persons (140 patients, 40 normal controls), to whom tablets of acetylsalicylic acid (aspirin) had been administered. The phenomenon was reproducible in patients who showed it, and the alternation of aspirin with sodium salicylate was followed by the appearance and disappearance of the occult blood from the stools. Aspirin in powder form gave similar results. The amount of aspirin taken had little influence on the occurrence of occult blood in the stools. From the strength of the reaction, and from spectrophotometric determinations, it was shown that the positive benzidine reaction was indeed due to blood, and that up to 4 ml. a day might be lost in this way. This figure exceeds the normal blood loss of menstruating women and may be significant in the production of anaemia in rheumatoid arthritis.

Other speakers were Drs. H. A. VALKENBURG and C. A. DE MOS on the latex fixation test; Dr. J. A. SZIRMAI on the dye uptake of acid polysaccharides; Drs. A. VAN DEN HOOF, W. HIJMANS, and M. J. W. KASTELEIN on the ultramicroscopic structure of L-forms of β-haemolytic streptococci; and Dr. J. M. F LANDSMEER on the functional anatomy of the finger.

NATURE OF STRESS DISORDERS

SOCIETY FOR PSYCHOSOMATIC RESEARCH

[FROM A SPECIAL CORRESPONDENT]

Many discussions on psychosomatic disease and stress disorder are made tedious by endless disputation on whether this or that disorder is psychogenic or organic, and what are the relative contributions of psyche and soma in each case. The very terms of such a disputation conceal the eventual truth that all clinical disorders are of multiple aetiology and all patients are people. The conference on "The Nature of Stress Disorders" organized by the Society for Psychosomatic Research, and held at the Royal College of Physicians from May 2 to 4, was refreshingly free from such red herrings.

A distinctive feature of the conference was the diversity of disciplines represented. From the medical side there were not only psychiatrists and physicians but also paediatricians, surgeons, dermatologists, gynaecologists, industrial and Service medical officers, and those whose work is in social medicine, student health, and anthropometric research. On the non-medical side were psycho-analysts, zoologists, anthropologists, and physiologists. With such a mixture there were necessarily occasions when communication broke down and the language of one was not understood by the other; but the increased range of perception well compensated. The chairmen of the various sessions were Dr. Charles Newman, Professor J. Z. Young, F.R.S., Professor Leslie Banks, Professor A. V. Neale, Dr. J. Fraser Roberts, and Dr. John Hambling.

Hypertension, Itching, and Dyspepsia

The conference was opened by a discussion of three somatic conditions in which stress is commonly thought to play a substantial part; essential hypertension, itching skin disorders, and dyspepsia. Dr. JOHN HAMBLING gave an account of investigations into the fluctuations of diastolic blood pressure over the course of psychiatric interviews, which demonstrated the abnormal degree of lability in these subjects. Rises in the diastolic pressure were particularly associated with the discussion of matters and persons about which the subjects had ambivalent and aggressive feelings. In the discussion, Mr. JOHN SOPHIAN quoted work and showed slides to demonstrate how ischaemia of the renal

cortex could be produced in experimental animals by exposing them to fearful situations or to selective brain stimulation, and suggested that herein lay a possible mechanism for the production of hypertension from psychological stress via the kidney.

Dr. BRIAN RUSSELL spoke on itching skin disorders, demonstrating the common cycle of scratch–itch–scratch lesion with particular reference to how psychological stress often initiated it. In discussion later, it was noted that the scratching component of these conditions could put them on a par with certain other motor psychosomatic disorders like tics, stammers, and the occupational cramps; it was suggested that some deconditioning techniques might be a useful adjunct to physical treatments or to psychotherapy here.

Dr. DESMOND O'NEILL reviewed the features of dyspepsia which could justify it being regarded as a stress disorder. He noted the changes in our ideas about this and kindred conditions, and made the point that a new taxonomy of disease was needed to match our changed views on aetiology; it would be, he thought, a taxonomy based upon reaction patterns. In discussion, it was noted how diagnostically typical were the personality factors in ordinary dyspepsia and duodenal ulceration; their absence alone was sufficient ground for suspecting neoplasia or other organic lesion. The conference was reminded how very far, in society, our dietary habits and widely spaced meals had departed from those of the omnivorous foraging ground ape which was our nature. The high incidence of dyspepsia, perhaps 20%, could be better understood if it were seen not as a departure from normality but as a failure to adapt to essentially unphysiological conditions. Menstrual disorders were the only other so-called stress conditions with an incidence comparably high, and here again the rarity of pregnancy in modern society was unphysiological. Dr. E. B. STRAUSS put in a plea for further work on what he termed human ethology,* so that we might know more of the occurrence of instinctual behaviour and displacement activity in socially inappropriate settings. He believed this would have a substantial bearing on the manifestations of stress disorder.

Salutary and Noxious Stresses

Group Captain V. H. TOMPKINS opened the next session with a paper on flying stress. The incidence of breakdown in flying personnel was surprisingly small. Where it did occur, fear seemed to be the principal causative factor; Group Captain Tompkins demonstrated a regular correlation between the casualty rate in different types of combat flying and the breakdown rate of the crews concerned. It was noted in discussion, both of this and other more theoretical papers, that there was by no means a constant correlation between overt environmental adversity and the manifestation of stress disorders; indeed, sometimes there seemed to be a negative correlation. Environmental adversity could be met, and there were well-recognized physiological mechanisms of adaptation to help. It was internal stress, often the product of unconscious motivation or anxieties, that more often seemed to result in maladaptive symptoms. Dr. J. SANDLER illustrated this by the detailed presentation of a case of vaginismus treated psychoanalytically. This patient had been reared in an aggressive, antagonistic family *milieu*; in her life-pattern she sought out, and was sustained by, aggressive, antagonistic relationships which would have seemed highly stressful to ordinary subjects.

Dr. J. J. O'DWYER, of Unilever Ltd., discussed the growing recognition of stress disorders as an important factor in industrial health and efficiency. Dr. NICOLAS MALLESON read a paper on stress in university students, showing how in this highly specialized group, with intensive medical supervision, up to 25% sought help for stress symptoms, mostly of a minor character and closely related to examinations. Whilst students with serious psychiatric disturbances carried an extremely poor academic prognosis, those seeking help for the lesser stress symptoms did considerably better than average. In discussion, it was suggested that perhaps some stress-induced distress was the inevitable price of social progress, and here, in microcosm, was an example of that principle.

Papers were also read on physiological stress, on experimentally produced stress, on genetic and constitutional factors in psychosomatic disease, and on stress in childhood.

General Conclusions

The final session was devoted to general conclusions. Dr. JOHN WISDOM, of the Department of Philosophy of Science, London School of Economics, opened with a remarkably tidy summing-up of what had been a very free-ranging conference. He classified the degrees of confidence with which different hypotheses in the field had been and could be established. The conference had shown a substantial measure of acceptable agreement on the occurrence and form of stress disorders; but very little was known about mechanisms, psychic or physiological—nor were they even convincingly speculated upon. In the final discussion several speakers noted that confusion of terminology had often produced confusion of thought; in particular the terms "stress disorder," "psychosomatic disease," and "psychoneurosis" had often been used synonymously, and needed clearer definition. Dr. J. N. MORRIS was struck by how little physiologists and psychologists in Britain co-operated in research; we were behind both East and West in this. The sociologist, too, he thought, had been reticent in turning attention to this field.

The conference had been generously supported by Genatosan Ltd., who are to meet the cost of publishing a volume containing both the papers and the discussions.

*See also the paper by Dr. John Bowlby read at last year's annual conference of the British Psychological Society (*Journal*, April 20, 1957, p. 941).

Motoring News

SOME FOREIGN CARS

In addition to the popular new British cars on the market there are a number of excellent products from abroad. Though slightly more expensive than the products of our own factories on account of import duties, they do offer exclusiveness and individuality, which is surely something we all crave in these days of mass production. With the present high purchase tax and increased labour charges a motor-car is a much more costly item to buy than it ever was before the war, even when the value of the pound is taken into consideration. Gone are the days of the £100 Ford and the £159 Hillman Minx, and they will probably never return. To obtain exclusiveness to-day, however, one really requires about £1,200, but it is possible to make a start with £796, the price of a Renault Dauphine, though this too is fast becoming popular on British roads. The next step up is the Fiat 1100, followed closely by the Simca Aronde. These cost £869 and £889 respectively.

The Dauphine is a very lively little car which can achieve over 40 m.p.g., and has excellent road-holding and suspension, the latter being rather firm for comfort on rough roads, however. The back seat is not particularly roomy for passengers with long legs, and the body is rather "tinny"; but, like all French and Italian cars, the money is spent on the works and not on the trimmings, with the result that this little car of only 8 h.p. by the old British standards is enormous fun to drive, is economical, has a truly capacious luggage compartment at the front, and is, of course, slightly unusual. The Fiat 1100 is roughly equivalent in size and capabilities to the Hillman Minx, but it has better suspension for cornering and more precise steering. The 1100TV was an improved version giving increased performance, but production of this has now been suspended. The standard production models cost £869, though a dual-purpose car is available at higher cost. The Simca Aronde is the cheapest four-door saloon in the range, the two-door versions, contrary to current practice, costing considerably

more. The Aronde is a fine all-purpose car with comfortable seats and sufficient leg-room in the rear for comfortable long-distance family motoring. Cruising speeds of 65–70 m.p.h. are easy, while a true maximum of 75 m.p.h. is available, with 60 in third a useful feature. Petrol consumption works out at 30 m.p.g. for touring. This Aronde is a very willing performer, and unlike so many of the Continentals it is not appreciably noisy. The steering column gear change is firm and precise, while the suspension and steering are as good as one will find in any car costing under £1,000 and indeed better than many costing twice this amount. The Aronde Grand Large at £998 is a smart two-door model with attractive lines for those who can afford to be really distinctive.

Creeping up a little further on our price ladder we come to £952, the Peugeot 203. This is a graceful-looking quality car which has a quiet dignity of its own. The 203 has been in production for a number of years, and there are many thousands in service, as visitors to France will notice. All the Peugeots are noted for their excellent paintwork and the attention which is paid to detail, yet they are some of the most pleasant and easy-to-drive cars on the road. Notable for their economy, light steering, and suspension, which will make the best of pot-holes and twisting country lanes alike, they have much to recommend them. The larger model is the 403, which will set you back £1,195. British models come with imitation leather upholstery specially fitted for this country and in a pleasant range of pastel colours. If you want a sliding-roof version of the 203 you must accept a left-hand-drive model or have the roof adapted here. The full cabriolet is no longer available here or in France, and only the 403 carries a coupé body at a rather prohibitive price.

Coming into four figures, the first car is the German D.K.W. Those who remember the old twin-cylinder two-stroke-engined fabric models of pre-war days may not know that the present model, available in various body styles, is now very definitely a luxury car with all the quality trimmings. The three-cylinder water-cooled 896 c.c. two-stroke engine purrs away contentedly and silently, yet contrives to propel the car in a most forthright manner when required to do so. By reason of the fast-revving engine vivid acceleration may be had in the lower gears; in spite of the front-wheel drive the steering is very light, and the sensation of being drawn along by the front wheels instead of being pushed by those at the rear is very real. Petrol consumption is 27–28 m.p.g. For £1,264 you can go German again with the Borgward. This is a remarkable car for one which has only a 1½-litre engine, because it offers comfort in the grand manner for four or five with luggage room to match, a top speed of 85 m.p.h., and a petrol consumption of 28 m.p.g., or 30 if your petrified wife happens to be at the wheel. You can, in fact, have your cake and eat it with this car, which is beautifully finished, like all other German marques, and is endowed with extremely powerful 2LS hydraulic brakes.

Finally comes the D.S.19 Citroen, more as a controversial talking point than as a successor to one's present car, for at £1,726 the Citroen is not a bargain in the present-day market. Fitted with automatic clutch, assisted gear change, power steering, power brakes, and the ingenious Oleo-Pneumatic independent front and rear suspension, this latest product from France is technically many years ahead of its time. So unorthodox is its layout of controls that one has almost to learn to drive all over again to be able to handle it. The D.S. is superbly comfortable on even the roughest roads, for which one can adjust the suspension accordingly. It is eminently suitable for long-distance fast travel, though its acceleration is not brilliant because of its poor power–weight ratio. Top speed is in the region of 80 m.p.h., which takes a little while to attain even on a long straight, and for overtaking one has to drop down to second gear to accelerate with any real rapidity. Gear changes are made by moving a thin lever at the top of the steering-wheel similar to preselector layouts; changes cannot be hurried, however, and the car takes its time moving away from rest, a disconcerting feature in city traffic. The braking is effected by a small round knob in place of the familiar pedal; there is also a slight delay here too after you have pressed the knob, and it takes one a while to acquire confidence in the otherwise extremely effective anchors. The secret is not to stand heavily on the knob even in an emergency, for the system is so powerful that all four wheels can be locked solid very easily. In all, the D.S. is a remarkable car which is bristling with so many new features that it takes time to discover them all. It seems, however, that it is best suited to the long roads of its native country, where its effortless travel must surely be a most desirable asset.

IAIN GELLATLY.

APPROVED NAMES

The last supplement to the consolidated list of "approved names" (dated January, 1958) was published in the *Journal* of February 1 (p. 278). A new supplement, dated May, 1958, is printed below. Communications relating to "approved names" should be addressed to the secretary, British Pharmacopoeia Commission, General Medical Council, 44, Hallam Street, London, W.1.

Supplementary List

Approved Name	Chemical and Other Names	Notes
Chlorphenoctium amsonate	2: 4-Dichlorophenoxymethyldimethyl-*n*-octylammonium amsonate. (Amsonic acid is adopted as the trivial name for 4: 4'-diaminostilbene-2: 2'-disulphonic acid)	Bactericide and fungicide
Chlorproguanil	N^1-3: 4-Dichlorophenyl-N^5-*iso*-propyldiguanide "Lapudrine" is the hydrochloride	Antimalarial
Dextromoramide	(+)-1-(β-Methyl-γ-morpholino-αα-diphenylbutyryl)-pyrrolidine "Jetrium"; R.875	Morphine-like analgesic
Dimethicone	A polydimethylsiloxane	Skin-protective agent used in therapeutic barrier creams
Ethotoin	3-Ethyl-5-phenylhydantoin "Peganone"	Anticonvulsant
Hydroxychloroquine	7-Chloro-4-[4-(*N*-ethyl-*N*-2-hydroxyethylamino)-1-methylbutylamino]quinoline "Plaquenil" is the sulphate	Antimalarial; also used for lupus erythematosus and rheumatoid arthritis
Isothipendyl	10-(2-Dimethylaminopropyl)-10-thia-1: 9-diaza-anthracene "Nilergex" is the hydrochloride; "theruhistin" is the hydrochloride	Antihistamine
Levomoramide	(−)-1-(β-Methyl-γ-morpholino-αα-diphenylbutyryl)-pyrrolidine	Morphine-like analgesic
Norethisterone	17β-Hydroxy-19-norpregn-4-en-20-yn-3-one 17α-Ethynyl-17β-hydroxyoestr-4-en-3-one 17α-Ethynyl-19-nortestosterone "Norlutin"; "Primolut N"	Oral progestogen
Pecazine	10-(1-Methyl-3-piperidylmethyl) phenothiazine The name "pacatal" is applied to the hydrochloride and the acetate	Tranquillizer
Perphenazine	1-[3-(2-Chloro-10-phenothiazinyl) propyl]-4-(2-hydroxyethyl) piperazine "Fentazine"; "trilafon"	Tranquillizer
Phenactropinium chloride	*N*-Phenacylhomatropinium chloride "Trophenium"	For controlled hypotension during surgical procedures
Poskine	Propionylhyoscine "Proscopine" is the hydrobromide	Treatment of travel sickness
Racemoramide	(±)-1-(β-Methyl-γ-morpholino-αα-diphenylbutyryl)-pyrrolidine	Morphine-like analgesic
Ristocetin	Antimicrobial substances produced by *Nocardia lurida* "Spontin" contains Ristocetin A and Ristocetin B	Antibiotic (effective against a wide range of staphylococcal and pneumococcal infections)
Salinazid	*N-iso*-Nicotinoyl-*N'*-salicylidenehydrazine "Nupa-sal"	Treatment of tuberculosis
Sulphaproxyline	N^1-(4-*iso*Propoxybenzoyl)-*p*-aminobenzene-sulphonamide	Sulphonamide
Tacrine	5-Amino-1: 2: 3: 4-tetrahydroacridine	Curare antagonist
Triamcinolone	9α-Fluoro-11β: 16α: 17α: 21-tetrahydroxypregna-1: 4-diene-3: 20-dione 9α-Fluoro-16α-hydroxyprednisolone "Aristocort"; "ledercort"	Anti-inflammatory glucocorticosteroid
Tropigline	Tiglyltropine	An atropine-like substance used in the treatment of Parkinsonism

To-day's Drugs

Under this heading we hope to publish from time to time authoritative notes on a selection of new drugs.

Vandid (Savory and Moore Ltd. for Carnegies of Welwyn Ltd.).—Vandid, vanillic acid diethylamide, is a central respiratory stimulant, similar in its mode of action to nikethamide, and 15 times as powerful in the morphinized animal. Its action is immediate, reaching a maximum within 1 minute, and passing off after 10 minutes. It is tolerated in at least four times the therapeutic dose. It is supplied as a 5% solution in 5-ml. ampoules and in dropping-bottles for oral use, and in 20-mg. tablets.

Vandid is indicated in cases of poisoning by barbiturates, coal gas, alcohol, and morphine. 10 ml. of 5% solution should be injected intravenously and 5 ml. intramuscularly every 3–4 hours until the patient is aroused. It may also be used to reverse the action of barbiturates used as anaesthetics. For circulatory support in diseases such as pneumonia, 1–2 ml. is injected, or 20–30 drops or 2 tablets given orally, several times daily. As a cardio-respiratory stimulant for premature or full-term babies with asphyxia or cyanosis, 0.2 ml. is injected or 2–3 drops are given orally every 2–4 hours. It may be given for several weeks to premature babies with cardio-respiratory inadequacy.

Sedumax Tablets (Calmic Ltd.).—Each tablet contains carbromal 120 mg., bromvaletone 120 mg., phenacetin 180 mg., aneurine hydrochloride 2 mg.

Both carbromal and bromvaletone are monureides. Urea itself is not a central depressant, but its substitution products have a hypnotic action. Carbromal was originally introduced with the idea that it would combine the sedative effect of bromine with the narcotic action of the aliphatic series, but the bromine component can hardly play any part in the action. Carbromal and bromvaletone are mild, innocuous, but rather inconstant hypnotics. The analgesic effects of phenacetin on headaches, migraine, dysmenorrhoea, and neuralgia are well known. A combination such as this may therefore be calculated to have a mild sedative analgesic action. The reason for the inclusion of aneurine in the preparation is less clear. Presumably it is included owing to the belief that vitamin B_1 has a beneficial effect on the neuritic pains commonly encountered in Great Britain—a common error for which there is no justification.

Spastipax Ionexten Tablets (Clinical Products Ltd.).—Each tablet contains the resin-bonded equivalent of hyoscyamine sulphate 0.35 mg., atropine sulphate 0.05 mg., hyoscine hydrobromide 0.025 mg., amylobarbitone 65 mg.

Drugs compounded with appropriate ion-exchange resins are inert except in the presence of free ions. In digestive fluids the resin compounds slowly and evenly release the active drugs over about eight hours, providing a constant therapeutic effect for ten to twelve hours from a single dose. Both atropine and hyoscine are parasympatholytic drugs, widely used as antispasmodic agents for gastrointestinal disorders. If given in sufficient dosage they should theoretically cause a complete block of the cholinergic innervation of the viscera. In practice they only antagonize rather incompletely the effects of vagal impulses, but they are nevertheless of some value in all types of visceral spasm. In addition hyoscine has a sedative effect on the central nervous system which would be potentiated by the amylobarbitone included in the preparation, and hyoscine is used for this purpose in the prevention of travel sickness and in the treatment of parkinsonism.

Owing to financial difficulties the Foot Health Educational Bureau will cease its activities, and for the present revert to the position of a standing body within the Central Council for Health Education.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Tetanus Immunization

SIR,—It is perhaps not generally realized that considerable sections of the civil population have received and are receiving active immunization against tetanus. These sections include: (*a*) Those young men who have completed their National Service. (*b*) The increasing number of young children who are immunized with "triple antigen." (*c*) An appreciable number of older children from independent schools where routine active immunization is practised.

In the event of injury these individuals should be given a booster dose of tetanus toxoid. It is unnecessary and indeed undesirable to run the risk of sensitizing them to horse serum by administering A.T.S. Members of my association do their best to instruct actively immunized individuals that they should ask for toxoid in place of A.T.S. if they are the victims of an accident. Nevertheless it has been found that this request is all too frequently disregarded, particularly in busy casualty departments, and A.T.S. is given willy-nilly.

I have been instructed by my council to bring this point to the attention of the profession through your columns. We would wish that all individuals who are actively immunized should be clearly instructed that they have received *toxoid* and are to ask for this to be repeated if they sustain an injury. On the other hand, we invite casualty officers and others to bear in mind the increasing possibility that the patient has been actively immunized, to ask in every case of injury if this is so, and if the answer is in the affirmative to administer toxoid rather than A.T.S.—I am, etc.,

London, W.1. THOMAS L. SCOTT, Hon. Secretary, Medical Officers of Schools Association.

Management of Tetanus

SIR,—The report of recovery in two severe cases of tetanus presented by Drs. R. S. Packard, T. B. Cartmill, and J. G. Henry (*Journal*, January 16, p. 16) is very encouraging. Tetanus is a serious problem in underdeveloped countries where treatment with relaxants, artificial respirators, etc., is usually not available. If the findings of Dr. Packard and his colleagues could be confirmed in a larger series of cases it would be a great advance in this otherwise serious, painful, and often fatal condition. Encouraged by their report I have recently treated a case of tetanus where the response was very heartening and recovery was rapid.

An 8-year-old boy was admitted on February 22, 1958, with fever and inability to open his mouth for the past 24 hours. He also complained of pain in the abdomen arising from the suprapubic region and going up to the epigastrium. Pain recurred every 4 to 10 minutes. There was no vomiting or other bowel disturbance. The boy had a discharging left ear and he remembered having inserted into his ear a stick which he had picked up from the roadside. He had a temperature of 100.2° F. (37.9° C.), pulse 120 per minute, and generalized rigidity of his muscles, particularly the abdominal muscles, and those of the neck, back, and legs. There was slight ptosis of the left eye. Jerks were exaggerated and ankle clonus was present on both sides. Trismus was marked and he could barely open his mouth 0.5 cm. Now and then violent spasms occurred and he went into opisthotonos. Under 10 ml. of intramuscular paraldehyde lumbar puncture was attempted unsuccessfully. Urine showed a trace of albumin, and the blood showed a mild degree of anaemia with a total W.B.C. count of 13,800 per c.mm., 74% of which were polymorphonuclear cells. He had a central perforation of his left eardrum and the ear discharge grew *Pseudomonas pyocyanea*. He was immediately given 300,000 units of A.T.S. in equal doses through intravenous, intramuscular, and subcutaneous routes. He was put on potassium bromide and chloral hydrate, each 0.5 g., and 50 mg.

of chlorpromazine three times daily, and was also given 200,000 units of sodium penicillin three-hourly. It was intended to increase the dose of chlorpromazine the next day, but the response was so good that this daily dose of 150 mg. was maintained. Within 24 hours his spasms had stopped and did not recur. Rigidity, however, persisted for much longer. The next day he could open his mouth better and rigidity had decreased slightly. 300,000 units of A.T.S. was given again, but was not repeated after that.

On the fourth day his temperature dropped to normal and remained so. Progress was maintained. Rigidity went on decreasing; convulsions did not occur, and on the ninth day he could walk with a stiff gait and a rigid attitude. His mouth could be opened fully. Ptosis had disappeared. He continued to make progress and was discharged on the 19th day (March 12, 1958), having fully recovered from his tetanus. Besides some Parkinsonian rigidity and flexion attitude he showed no signs of toxicity. Chlorpromazine was stopped two days before discharge.

It could be argued that the recovery was probably due to the large dose of A.T.S. used (total of 600,000 units), but I feel that the recovery was due more to the use of chlorpromazine. I have seen identical cases of tetanus where doses of A.T.S. of a similar order have been used without any beneficial effect. The marked effect on convulsions was very striking. Evidently this case was not severe, but it is difficult to say what the outcome might have been with conservative management without the use of chlorpromazine. It is possible that the case might have recovered, but suffering would have been great. Chlorpromazine, by abolishing convulsions, reduced the misery of disease, conserved the energy of the patient, and thus accelerated the recovery.

It is interesting to note that my patient also developed a mild Parkinsonian syndrome like the second case of Packard *et al.* The total dose of chlorpromazine used in their case was 2,925 mg., whereas in my case it was 2,550 mg. It is probable that this toxic side-effect will be seen more often where there is already a toxi-infective disorder of the nervous system.

I am indebted to Lieutenant-General W. A. Burki, D.G.M.S., and Major-General M. N. Mahmood, D.M.S., for their kind permission to report this case.

—I am, etc.,

Peshawar, West Pakistan. M. B. AZAMI.

Out-patient Gynaecology

SIR,—The article on this subject by Drs. Norman Morris and Desmond O'Neill (*Journal*, May 3, p. 1038) makes depressing reading for the scientifically minded gynaecologist. The authors conclude, in effect, that if a physical cause for a symptom does not obviously present itself, then the basis is psychological, and they conclude that this factor is responsible for the disabilities of roughly 60% of gynaecological out-patients. One's first reaction to this statement is that the women who go to University College Hospital must be a peculiar lot, for a recent survey of 15,000 patients attending my own clinics at five widely separated London hospitals gives "psychological" as the diagnosis in only 0.3%. The discrepancy, of course, arises from the difference in the interpretation of symptoms, and here I must take radical issue with Drs. Morris and O'Neill.

It is of course true that emotional factors exaggerate physical symptoms, particularly pain, and may even cause some menstrual irregularities such as amenorrhoea. (The suppression of menstruation by the unfounded fear of pregnancy is a well-known example of the latter.) But I have always found it difficult to believe that emotional stress alone can actually *initiate* gross symptoms, particularly pain. The basic essential must surely be either a pathological peripheral organ or a fault in the transmission pathway. One has only to sit down and try to *imagine* a pain in a healthy organ to appreciate the difficulty. I myself have always found it impossible, even with the utmost concentration, and I cannot believe that the average woman, however tangled her domestic affairs, can do any better. Some of the very cases cited by the authors bear out this contention. In Case 3 the "emotional component" is assessed at 100%, but is it not more likely that the abdominal pain and generalized rash were due to the "dettol" she had drunk, rather than to dislike of her husband? Case 42 developed dysmenorrhoea on coming to London and conducting an affair with a married man. But this was three years after her menarche, the usual time of onset of this symptom. Was not the establishment of ovulation the more likely cause?

I have shown repeatedly, not by psychological guesswork but on the firm basis of serial microscopy, that pelvic pain is primarily due to pathology, either in the viscera concerned or in their supplying nerves, and that the appropriate operative treatment will cure the majority of cases. Similarly physiotherapy will relieve much of the backache due to the pelvic joint disorders of the parous woman. The often excellent result of short-wave diathermy in local inflammatory disease in the pelvis is well known, even when physical signs are minimal, and there are few "functional" menstrual disorders which cannot be regulated by curettage and hormone therapy. If the majority of these troubles are due to emotional stress, and that is what Drs. Morris and O'Neill claim, why do they react so well to purely physical treatment?

The answer surely lies in the problem of adequate diagnosis, an admittedly difficult one in the absence of gross pathology. The fact that obvious changes are not immediately apparent on bimanual palpation does not eliminate the possibility of some minor disorder, and closer local search for the cause of symptoms should precede their final relegation to the imaginative cortex. Colposcopy, the vaginal smear, fluoroscopy, and hormone estimation will establish a cause for many minor gynaecological troubles, and simple *physical* measures (including minor neurosurgery) will relieve most of them. The whole drive of modern medicine has been in the direction of better physical diagnosis. It would indeed be a great pity if this were slackened in gynaecology, as it must inevitably be if the authors' contention that most pelvic symptoms are of emotional origin was allowed to pass unchallenged.—I am, etc.,

London, W.1. ALBERT DAVIS.

SIR,—The paper by Drs. Norman Morris and Desmond O'Neill (*Journal*, May 3, p. 1038) in which they state that "emotional tension outweighs physical malfunction and disease as a cause of illness in women who attend a gynaecology clinic," brings to my mind an incident in out-patients 20 years ago. The consultant was asking us students the treatment of dysmenorrhoea. All the usual ones had been given and at my turn I knew the answer: presacral sympathectomy was all that was left. Instead I said: "Send her to a psychiatrist, Sir." There was a shocked silence, some titters, and the great man's mouth fell open. I shall never forget his withering scorn as he said: "Send my patients to a psychiatrist—do you think I want them to come back to me with straw in their hair?" I had to wait 20 years for Dr. Morris and Dr. O'Neill to vindicate me.—I am, etc.,

London, W.1. GORDON AMBROSE.

Dirty Habits

SIR,—I wish, by the following experience, to support the excellent letter of Dr. Jno. Crawford, published under the title "Dirty Habits" in the *Journal* of April 19 (p. 943), in which he urged that a Government publicity campaign be launched to impress upon the public the importance of acquiring the simple and elementary habit of washing one's hands after using the lavatory.

A few days after reading this letter I had occasion to use a public lavatory at one of London's main railway termini. To do this I had to pay the customary penny, but in order to wash my hands afterwards I had to pay 4d. Such a procedure can hardly be said to encourage anyone to adopt this necessary hygienic measure. I would suggest that as a first step in public education on this matter all washing facilities in public lavatories should be seen to be adequate and, in addition, should be free of charge.—I am, etc.,

London, S.E.13 J. P. GREAVES.

SIR,—Children should of course be taught to wash hands after going to the lavatory, as Dr. Margaret P. Cosham suggests in your issue of May 3 (p. 1062). However, the

conditions in many of our older schools make this very difficult if not impossible.

My mother was headmistress of a small rural school in the South, and she had a long hard fight lasting several years before earth closets were replaced by flush lavatories, and wash-basins for the children's use were fitted. I myself have been teaching in a down-town school (built 1874) where water for the infant children had to be fetched from one cold tap in the staff-room. Regular hand-washing was impossible except before dinner, and then a number of children had to share the same bowl. In addition the weekly supply of towels was quite inadequate. It would appear that some of the publicity in this matter might be directed towards those responsible for our schools, so that reasonable facilities should be provided in *all* school buildings.—I am, etc.,

Sheffield, 10. WYNEFRED HIGGINBOTTOM.

SIR,—We should be grateful to your correspondents (*Journal*, April 19, p. 943, and May 3, p. 1062) for drawing attention to the need for public education in the matter of hand-washing, but in their pleas for a publicity campaign they have overlooked the work that has been done for many years, and which is being carried out at this moment, by public health departments supported by the Central Council for Health Education.

Clean food campaigns and clean food guilds have been prominent amongst the activities of local authorities for some years, and courses of instruction for food-handlers are usually an important feature. The specific advice "Now Wash Your Hands" is contained on metal plaques or labels affixed to lavatory doors and other appropriate places, and since January, 1956, alone the Central Council for Health Education has supplied 35,500 metal plaques and 315,000 labels, not only to local authorities, but also to banks, hostels, and industrial organizations. Dr. Margaret P. Cosham's protest that there has been legislation without education (*Journal*, May 3, p. 1062) is unjustified. The requirements concerning washing facilities which she mentioned are laid down in regulations made under the Food and Drugs Amendments Act, 1955, which came into force in January, 1956. Under these regulations it is now obligatory for catering establishments to display the "Wash Your Hands" notice. Within three weeks of the publication of these regulations the Central Council for Health Education, anticipating the needs of local authorities and caterers and all branches of industry, published an illustrated and simplified booklet, *Your Guide to the Food Regulations*. Shortly afterwards, a wall poster summarizing the requirements of these regulations and simply illustrated was also published. Since that date the Central Council for Health Education have supplied 200,000 booklets and 7,000 posters to local authorities for distribution to the catering trade and also to industrial organizations and other interested bodies.

Realizing that the human hand is the important factor of food infections, the Central Council for Health Education produced several years ago a visual aid for use in schools and in courses of instruction for food-handlers in which a red hand is shown to be a central point of a "vicious circle," which is in fact the name of this teaching-aid. Once again, taking January, 1956, as a baseline, this Council has supplied 600 copies of these teaching-aids to local authorities and also to industrial organizations.

Therefore there has been a substantial effort in publicity, and it would be difficult to accept the examples quoted by your correspondents suggesting that this publicity has had no effect. The very fact that Dr. Sylvia D. Chapman can find a shop that used tongs (*Journal*, May 3, p. 1062) shows that the message has got home. Additional evidence is supplied as when commerce has been enterprising enough to produce new appliances and aids to assist in carrying out the principles of clean food-handling.

This is not to say that the time has arrived when we can relax our efforts—the case quoted by Dr. Chapman is evidence of this, although the returns for food poisoning to the Ministry of Health are evidence enough. On the other hand, it would be wrong for your readers to be left with the impression that nothing has been done and that those who are primarily concerned are not fully alive to the importance of this aspect of epidemiology.—I am., etc.,

London, W.C.1. JOHN BURTON,
Medical Director,
Central Council for Health Education.

School Medical Inspections

SIR,—Dr. J. A. H. Lee's article "The Effectiveness of Routine Examination of Schoolchildren" (*Journal*, March 8, p. 573) might have been more accurately entitled "The Effectiveness of Documentation in the School Health Service." Personally, I think that the "yardstick" he has chosen is inappropriate, and one which could be bettered. After more than ten years' experience as a school medical officer, I am convinced that a routine medical inspection affords a quick and effective assessment of a pupil's health, and gives satisfaction to most parents. I am sure that most of us would welcome half an hour instead of ten minutes for examinations, but even although attempts were made to recruit larger staffs I doubt if doctors of the best calibre would come forward unless great improvements were made in the status and salary scales of the school medical officer.

While a shadow has been cast over the School Health Service it appears that the general practitioner also comes under fire, for Dr. Lee cites in detail eight cases of missed cardiac defects, yet in only one of these is the family doctor mentioned. Surely the majority of children have a chest auscultation, for one reason or another, by the family doctor before they attain school-leaving age.

Reference has been made to the doctor–patient relationship, but in the School Health Service I would lay more stress on the doctor–parent relationship. When parents approach one in the streets, in shops, by telephone, and even, on occasion, at kirk on a Sunday, to discuss their child's health, I feel pleased to think that the public has such confidence in its School Health Service.—I am, etc.,

Kirkcaldy, Fife. J. A. PETRIE.

Intra-articular Injections for Arthritis

SIR,—I was extremely interested to read of the investigation carried out by Dr. K. A. Ross and his colleagues on the treatment of osteoarthritis of the knee by local injection of salicylate compounds (*Journal*, May 3, p. 1040). Reference is made to the short series I published in 1945.[1]

I have continued to use these preparations in the treatment of the osteoarthritic knee in some 400 to 500 cases. I can fully endorse the efficacy of the method, my original figure of 80% of favourable responses having been maintained. A follow-up of some of the satisfactory cases has shown that the disease does not appear to return in a proportion of these, provided it was not too advanced when originally treated.

I have seen a number of patients in which one knee was treated and became symptom-free, but who returned some years afterwards with the disease in the other knee, the treated knee not having relapsed, however. With regard to the osseous injections, I must confess to having been disappointed with the results obtained. It is true that I used much smaller quantities of the solution and did not use hyalase.—I am, etc.,

London, W.1. A. C. ELKIN.

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1 Elkin, A. C., *Med. Press*, 1945, 213, 350.

SIR,—The use of intra-articular injections for rheumatic diseases appears to be increasing, whether these be of hydrocortisone or lactic acid, especially in orthopaedic outpatient clinics. A number of medical officers-in-charge have told me that following the use of hydrocortisone they have reverted to lactic acid, especially in the treatment of the larger joints, as the results were better. I am at present trying to estimate the effects of the two substances in the way of improvement in comparable cases, but, as I fear that I may be unconsciously prejudiced in favour of lactic acid, I would be grateful if any practitioner who has had the opportunity of using both substances for injection would communicate with me and let me know his opinion, particularly in comparable series.—I am, etc.,

10, Grange Terrace, Sunderland W. GRANT WAUGH.

Blood Folic Acid

SIR,—Drs. H. Baker, H. Ziffer, I. Pasher, and H. Sobotka (*Journal*, April 26, p. 978) record a series of blood "folic-acid" levels. Similar efforts to measure the folic-acid content of plasma, serum, or whole blood were made by Schweigert and Pearson,[1] Wolff, Drouet, and Karlin,[2] Spray and Witts,[3] Toennies, Frank, and Gallant,[4] and Nieweg, Faber, de Vries, and Kroese.[5] It is, however, unlikely that what is being measured is, in fact, folic acid.

Folic acid is estimated by microbiological assay, and the presence of serum or blood haemolysates may stimulate some growth of the folic-acid-dependent mutants of *Streptococcus faecalis*, *Lactobacillus casei*, and *Bacillus coagulans* which are used in these assays. There is, however, no evidence that this slight growth reflects the presence of pteroylglutamic acid (folic acid) in these blood samples.

(1) The folic-acid requirements of these organisms may be replaced by various purines and pyrimidines, sometimes by *para*-aminobenzoic acid, as well as by various folic-acid analogues.

(2) Usdin, Phillips, and Toennies[6] analysed "microbiologically active" fractions in whole blood by paper electrophoresis and chromatographically and were unable to demonstrate the presence of folic acid, folinic acid, or any related compound.

(3) Folic acid itself probably has no physiological function. The form active in the transfer of single carbon units is probably related to N^{10}-formyltetrahydropteroylglutamic acid, which is highly unstable.[7]

(4) Sensitivity to folic acid has been reported in a normal subject.[8] This subject at least had no folic acid in his plasma and he did not develop signs of folic-acid deficiency.

Vitamin B_{12} is unique among the vitamins in that it is carried in plasma bound to a specific α-globulin, and this binding of B_{12} in plasma is responsible for the presence of a significant serum level. No such situation prevails in relation to folic acid. There is, therefore, no evidence for the presence in fasting blood of measurable amounts of folic acid and related compounds.—I am, etc.,

London, W.12. I. CHANARIN.

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Cases of Acrocephalosyndactyly

SIR,—I am investigating the aetiology of acrocephalosyndactyly and am anxious to obtain further cases of this congenital abnormality.

Acrocephalosyndactyly is most conspicuously a malformation of the osseous system, recognizable at birth and characteristically affecting the skull, hands, and feet (see Figure). The most obvious features are an abnormally shaped cranium and face (associated with early and irregular obliteration of one or more sutures) with syndactyly of hands or feet or of both. The cranium is short, broad, and high. The occiput is flattened and forehead unusually vertical. In infants the fontanelles may be very large, and a prominent swelling is often seen in the region of the metopic suture. The maxillae are hypoplastic, giving the face a flattened appearance. Proptosis, strabismus, and relative prognathism of the lower jaw are generally seen. The palate has a high roof and is frequently cleft. In the upper jaw the alveolar borders are thickened and the teeth crowded. The syndactyly may vary from a pronounced osseous union of digits, metacarpals, and carpals (or metatarsals and tarsals) to minor soft-tissue syndactyly. In addition to these cardinal features, abnormalities of other systems are frequently found.

Probably the majority of these cases do not survive the first few days of birth, and I should like to ask whether any of your readers can recall a patient with this anomaly. If so, would they be kind enough to contact me? I am particularly interested in the family history of cases dying in early infancy.—I am, etc.,

The Galton Laboratory,
University College,
London, W.C.1. C. E. BLANK.

The Harvard Step Test

SIR,—There appears to be some disagreement among experts as to how this test should be conducted. Schneider and Karpovich[1] and Morgan and Adamson[2] state that pulse readings should be taken from 1–1½ min., 2–2½ min., and 4–4½ min. after 5 minutes of step-ups. Other authorities[3–6] quote the time for pulse readings as 1–1½ min., 2–2½ min., and 3–3½ min. It appears, therefore, that there are two separate tests. In an endeavour to find which, in fact, is the Harvard step test I wrote to the American Association for Health, Physical Education and Recreation, which confirmed that Dr. Lucien Brouha,[7] of Harvard University, advocates the second method quoted above.

It does not seem to matter much which test is used, as both are an effective way of measuring cardiovascular fitness. What does, however, matter is to know, when comparisons are being made between the physical fitness indices of well-known athletes, that the results quoted have been computed in the same manner if a fair comparison is to be made. I believe that the Amateur Athletic Association's coaches have been testing athletes in this country and using the first method of testing and not the recognized method of conducting the Harvard step test. A statement by the B.M.A. as to the correct method of conducting this test and computing the physical fitness index would be most welcome and a great help to physical educationists and athletics coaches.—I am, etc.,

Physical Education Department,
St. Luke's College, Exeter. W. R. CAMPBELL.

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Management of Hypertension

SIR,—The question asked by Dr. H. A. Reid about the indications for hypotensive drugs (*Journal*, April 12, p. 891) prompts the reply that hospital is not the place where the progress of hypertension can be adequately dealt with. For 27 years I have prevented damage from hypertension in all but the long-neglected cases by taking the B.P. of suspicious cases every month, or fortnightly if the B.P. has risen dangerously, and treating them promptly by rest when necessary. In general practice one can promise constant care, and so get co-operation in patients, who become interested instead of frightened. All this was done long before the new hypotensive drugs were discovered. The

only trouble was that extreme rises in B.P. had to be treated by three weeks in bed, which was unpopular, but did the trick, and next time there was less resistance.—I am, etc.,

New Milton, Hants. MARY G. H. EDWARDS.

Regressive Shock Therapy

SIR,—I am disappointed that the letter from Dr. M. G. Jacoby, of New York (*Journal*, February 1, p. 282), under the heading "Abuse of E.C.T." has until now aroused no comment. For those in mental practice his brief description of what he calls "regressive shock therapy" is surely of very great importance. Dr. Jacoby says, "In this form of treatment E.C.T. is given several times daily for ten or more days until the patient is so regressed that he is bedridden, does not know his name, is doubly incontinent, and is unable to swallow. This treatment is given to chronic paranoid schizophrenics who are completely out of contact." The method described has not received recognition by any British authors of standard works. Perhaps also it is to be regretted that Dr. Jacoby does not quote any references. He says the method is "rarely used, but valuable."

From personal experience of a related technique, I have no doubt whatever that Dr. Jacoby is well justified in claiming to have secured a number of recoveries with regressive shock therapy. I assume, since he does not state otherwise, that Dr. Jacoby uses "straight" or "one-shot" E.C.T.—i.e., the traditional method. If he were to use instead the "ectonus" technique, devised by Dr. R. J. Russell in 1956, he would find his results were even better. The method of applying ectonus in severe psychoses is, normally, to push this form of E.C.T. to the point of producing a confusional state in the patient. This can usually be achieved by seven doses of ectonus given as one dose per day on seven consecutive days. A confusional state which lasts on average for four or five days follows, but the patient is usually manageable and not doubly incontinent, and afterwards, apart from some transitory amnesia, is very well mentally.

In 1953 a method of intensified E.C.T., later described as fused-dosage or interrupted fused-dosage (I.F.D.), was outlined by Drs. R. J. Russell, L. G. M. Page, and R. L. Jillett.[1] Daily dosage to the point of producing confusion was clearly stated by these authors to be the aim of treatment. They stated also that the good results achieved were probably due to the fact that the patient had been rendered confused.

I suggest that this form of therapy is even more effective when the E.C.T. is either by the ectonus technique or I.F.D. and not "one-shot." Also I strongly recommend that in all severe psychoses the course of E.C.T. should be combined with a concurrent course of drugs of the promazine group —i.e., chlorpromazine, "notensil" (acetylpromazine), or "sparine" (promazine hydrochloride), or combinations of these. Daily dosage of 300 mg. of the promazine drug in the case of chlorpromazine or sparine, or 180 mg. if notensil is used, should be given for six weeks or more, with reduced dosage in the latter part of the course. This treatment, under the name ectonus-promazine therapy (E.P.T.), is fully described in a recent series of articles on new techniques in electroconvulsant therapy.[2] E.P.T. has given impressively good results in the treatment of chronic as well as recent schizophrenia and in other mental conditions. The promazine potentiates the E.C.T., making treatment effective with fewer doses of E.C.T. and conferring a quality of permanency on the therapeutic result.—I am, etc.,

Glasgow, W.2. ALLAN A. MACDOUGALL.

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Halothane Concentration

SIR,—I mentioned in a letter concerning the use of halothane (*Journal*, March 15, p. 644) that I considered it inadvisable to plug a Rowbotham's bottle into a circle absorption system so that a patient has to breathe through the bottle, as it was not designed for the purpose, and the resistance was too high. This advice is disputed by Dr. P. J. C. Burton (*Journal*, April 5, p. 831), who is under the impression that there is no more resistance in the Rowbotham bottle than in the ordinary ether vaporizer in the circuit. I will now give figures to show that I believe my advice to be well founded, and that there is very considerable resistance in this bottle.

The resistance to gas-flow in various pieces of anaesthetic apparatus can be compared by blowing air through them from a mechanical respirator.[1] The figures in Table I show the results

TABLE I.—*Comparative Resistance of Various Pieces of Anaesthetic Apparatus to Flow of Air From Beaver Mk. 1 Respirator: in mm. Hg to Nearest 0.25 mm.*

C.M. Mk. 1 absorber, lime on, ether off	1.5
" " " " " ether on	2.75
(Resistance attributable to ether vaporizer)	(1.25)
Rowbotham bottle, alone, "on"	12.5
" " " "off"	9.0
Rubens non-rebreathing valve: to expiration	4.75*
" " " " inspiration	2.0*
Standard endotracheal adapter, to inspiration	2.25
Macintosh's special endotracheal tube unit	1.25
Bullough's endotracheal connexion + size 12 E.T. tube	1.25
Parkinson gas-meter type spirometer	1.25
Soda-lime canister, with lime, from circle absorber	0.75
Standard length of hosing (according to diameter) large	0.25
" " " " " " small	1.0

*These figures are surprisingly high, as this valve is said to have little resistance.

of such a test, which speak for themselves. In this test the resistance in the Rowbotham bottle by itself is roughly ten times greater than that attributable to that in the standard ether vaporizer. The other figures are given for comparison and to show that properly designed apparatus need have only slight resistance at the gas-flow used, which is roughly two to three times that occurring in slow quiet breathing.

In another test the respirator was attached to a Coxeter-Mushin Mk. I circle absorber to form a mock-lung, and functioned just like a patient breathing through a face-mask as in clinical use. In this test (Table II) the figures are modified by the presence of

TABLE II.—*Resistance in Coxeter-Mushin Mk. 1 Circle Absorber During Mock-Lung Experiment with Beaver Mk. 1 Respirator: in mm. Hg to Nearest 0.25 mm.: to Expiration*

C.M. absorption unit, lime off, ether off	2
" " " " on, " "	4
" " " " " on	4.5
" " " " " " off + Rowbotham bottle "on"	13.0
" " " " " " " "off"	10.0

hosing, valves, bag, Y-piece, etc., which have their own resistance. The introduction of a Rowbotham bottle, as in clinical use, trebles the resistance in the circuit.

Those who believe, as I do, that resistance should be avoided will not use the bottle in this way. When the bottle is in use in a semi-open circuit, as in dentistry, it should be placed between the machine and the reservoir bag, and the bag should always be "on." I have seen severe dyspnoea when the bottle was on the wrong side of the bag in dental anaesthesia. As one of those who have on many occasions drawn attention to resistance in respiratory apparatus, may I plead for official standards to be laid down to which apparatus must comply before being offered for sale?

Perhaps I should add that the Rowbotham bottle is not involved in this matter, as it is intended only for the vaporization of liquid anaesthetics by gases coming from flowmeters, etc., and can, of course, be so used for delivering halothane to a circle absorption unit, if desired.—I am, etc.,

Chislehurst, Kent. JOHN BULLOUGH.

REFERENCE

1 Bullough, J., *Anaesthesia*, 1955, **10**, 183.

Carpal Tunnel Syndrome

SIR,—I was interested to read the letter by Mr. David A. Richmond (*Journal*, March 29, p. 773). After treating a number of cases of carpal tunnel syndrome by injections of hydrocortisone I found I obtained far better results by treating the condition as one of compression and tenosynovitis. In the last 20 months 49 cases were injected with 8 ml. of lignocaine and 2 ml. of hydrocortisone with gratifying results. 33 cases obtained complete relief; of the remaining ten, six only have occasional twinges, while the

remaining four have had to return after 4–6 months for similar treatment on one or more occasions. A further seven cases are now under observation. (One of these has so far failed to respond to the above treatment, while another has not returned after one injection.)

I wonder if the following observation has been noted by others of your readers. Out of the cases seen, all but one possessed a palmaris longus, although the latter is said to be absent in at least 10% of people. As this tendon is the only one attached to the carpal ligament, this might help in the compression of the tunnel, which would tend to support those who believe that many of these cases are due to chronic hyperextension of the wrist.

While I hope to write a more detailed account of my observations, I would like to take this opportunity of thanking my colleague Dr. Cedric Hirson, for his kind advice and for providing a large amount of the material.

—I am, etc.,

Carshalton, Surrey. A. A. VAN DER BRACHT.

Reserpine in Thyrotoxicosis

SIR,—I have read with interest your editorial comments on reserpine in thyrotoxicosis (*Journal*, February 22, p. 450). Nearly three years ago I referred to the use of *Rauwolfia serpentina* in thyrotoxicosis,[1] and since then found some degree of amelioration of symptoms in further cases of thyrotoxicosis. It appears not to be a specific treatment for thyrotoxicosis, and the drug may be considered as an "adjunct to treatment." I also noted mild water retention with its use. Later we referred to facial oedema and puffiness of the eyelids[2] with the use of reserpine.

Further, it was mentioned that Canary *et al.*[3] found that reserpine "did not significantly depress thyroid activity as measured by the uptake of radio-iodine or blood levels of protein-bound iodine." This view needs further confirmation, as E. Saarenmaa[4] observed in a study of 50 patients treated with reserpine that the fall in the level of protein-bound iodine was appreciable in those cases where it was pathologically elevated. It fell on the average from 8.5 γ% to 6.5 γ%. The drug was given orally in doses of 0.2 mg., three times daily, up to a total amount of 20 mg., and the level of protein-bound iodine was measured before and after the one-hundredth dose of reserpine.—I am, etc.,

Calcutta. A. K. ROY CHOWDHURY.

REFERENCES

1 Chowdhury, A. K. Roy, *Indian Practit.*, 1955, **8**, 777.
2 Chatterjee, R. N., Chowdhury, A. K. Roy, Mukherjee, M. M., and Das, T., *J. Indian med. Ass.*, 1956, **27**, 167.
3 Canary, J. J., Schaaf, M., Duffy, B. J., and Kyle, L. H., *New Engl. J. Med.*, 1957, **257**, 435.
4 Saarenmaa, E., *Acta chir. scand.*, 1957, **112**, 199.

Oestrogens in Osteoporosis

SIR,—Your leading article (*Journal*, May 3, p. 1051) raises the question of the carcinogenic properties of prolonged oestrogen therapy. You refer to the work by Henneman and Wallach,[1] who reported that only 4 out of 200 women suffering from post-menopausal and senile osteoporosis developed genital cancer after long administration of oestrogens. These authors conclude from their findings that this low incidence of cancer in women of the cancer age group does not justify the fear that prolonged oestrogen therapy may be carcinogenic.

In a recent paper[2] I pointed out that the incidence and severity of calcified atheroma of the abdominal aorta are considerably greater in females than in males in the older age groups. I found the most extensive calcification of the abdominal aorta in women with senile osteoporosis. According to my theory,[3] individuals with advanced calcified atheroma are relatively immune to cancer, in particular to cancer of the stomach and the sex organs. It is therefore suggested that, in the series of cases reported by Henneman and Wallach, calcified atheroma may have protected these patients from developing genital carcinoma, in spite of prolonged oestrogen therapy. Thus the evidence produced by these authors seems to be in support of my conception of a negative cancer–atherosclerosis relationship, but does not as yet exclude the possibility that prolonged oestrogen therapy may be carcinogenic in women more prone to develop cancer.—I am, etc.,

London, W.1. A. ELKELES.

REFERENCES

1 Henneman, P. H., and Wallach, S., *Arch. intern. Med.*, 1957, **100**, 715.
2 Elkeles, A., *Lancet*, 1957, **2**, 714.
3 —— *Brit. J. Cancer*, 1956, **10**, 247.

Post-operative Position

SIR,—I was delighted to see Mr. Geoffrey Housden (*Journal*, April 5, p. 830) supporting me in my recent tilt in a letter to the *Lancet* (December 21, 1957, p. 1290) against the mistaken belief that "early stagnation" is equivalent to "early ambulation."

To banish post-operative leg venous thrombosis from our wards needs the co-operation of the anaesthetist, the surgeon, and the ward sister, in that order. The anaesthetist is almost the most important person of all, for his task is to administer an anaesthetic from which the patient can be released the moment the operation is over, thus enabling the surgeon to drill (perhaps hypnotize would be a better term) a post-anaesthetically co-operative subject into flexing and extending the ankle-joint when he sees the patient. This is reinforced by sister and her staff during the next twelve hours, so that within a very short time we have a patient who is continually and automatically pumping up venous return from the leg.

The interval after an operation before which the patient is first allowed out of bed must surely depend upon the personal wishes of the surgeon, who will take into account the nature of the operative procedure he has performed. But with this method of "walking in bed" delay in ambulation on terra firma is of no thrombotic or embolic importance. When patients are eventually allowed up it should be to *walk* only, and it is best during the first 48 hours of ambulation to limit this to a maximum of 4 minutes every four hours. Walking does not mean shuffling about in slippers, it means wearing socks and well-fitting lace-up shoes so that every step pumps up venous return. I have no objection to patients sitting for a short time in a chair once they can walk well, provided they wear shoes, do not sit with their legs up on a stool or crossed, do not huddle around the ward fire, and above all do not forget to "walk" whilst they are sitting, as if beating time to music.

Surprisingly, perhaps, we do not expect our patients to "walk" whilst they are asleep. Nocturnal venous return is taken care of by the fact that the foot of the bed is permanently raised nine inches (23 cm.). I must emphasize that this is the minimum effective height, and indeed the benefit of this is lost if the patient sleeps with more than two pillows for the head.

As for results, I can only say that, loyally aided by my anaesthetist, Dr. Kennedy Harper, and by numerous floor sisters, I have not had a single post-operative venous thrombosis in the past ten years of vein surgery, despite the fact that many upon whom I operate have a history of deep venous thrombosis in the other leg. And I have been equally fortunate in those cases with a personal history of repeated thromboses and pulmonary emboli who need further surgery (e.g., herniae, gastrectomy) over whom I am from time to time asked to hold a watching (walking !) post-operative brief.—I am, etc.,

London, N.W.1. STANLEY RIVLIN.

SIR,—Stimulated by the recent interesting correspondence on the subject of post-operative position, begun by Dr. H. L. Marriott (*Journal*, January 25, p. 215), may I refer back to a letter of mine you printed some years ago (*Journal*, March 13, 1954, p. 643) and briefly report the results of the method of treatment there described? In 2,672 consecutive gynaecological operations since June, 1953, there has been one death from pulmonary embolism; this occurred on the fourteenth post-operative day following an extended radical excision of the vulva for carcinoma; during this period no anticoagulant drugs had been used.

This does not prove anything, as the figures are small and there is no concurrent control series, but during the previous three-year period when our standard post-operative position

was the left lateral, with flexion at the hip- and knee-joints, there were two deaths from pulmonary embolism after 1,531 operations, and the incidence of post-operative deep venous thrombosis was five times higher. The method has some teaching value too, for it is demonstrative and directs the attention of doctors and nurses to the care of the calf veins both in the ward and in the theatre. Keep the legs up!—I am, etc.,

Great Baddow, Essex. ANTHONY C. PEARSON.

Rheumatology as a Whole-time Specialty

SIR,—Dr. W. S. C. Copeman (*Journal*, April 26, p. 1006) states that it is only in the N.H.S. that the need for special diagnostic and treatment facilities for sufferers from rheumatic disorders is not recognized. But surely he exaggerates? A start has been made in the N.H.S. After the publication of the Royal College of Physicians' report,[1] the North-east Metropolitan Regional Hospital Board established a central rheumatism centre and peripheral centres according to the recommendations of that report. All information regarding these centres is regularly circulated to all practitioners in the region. And has Dr. Copeman forgotten that he himself is senior physician to the Arthur Stanley Institute for Rheumatic Diseases, where he is employed under the N.H.S. in the North-west Metropolitan Region?—I am, etc.,

London, W.1. WILLIAM TEGNER.

REFERENCE

[1] Royal College of Physicians, *Report of the Committee on Chronic Rheumatic Diseases*, 1951.

First Tuberculosis Dispensary

SIR,—Drs. W. Hartston and W. F. Wheeler (*Journal*, April 26, p. 1005) should continue their interesting researches into London medical institutions of the Victorian Age. As they claim, this historical discipline is admirable. But to understand the difference between those "phthisical dispensaries" and the modern tuberculosis clinic requires something more—historical imagination.

Certainly, the infectivity of tuberculosis was surmised earlier than Robert Koch's discovery in 1882, yet before that date the idea was never applied, except as a measure of segregation. It remained for Sir Robert Philip to exploit Koch's discovery as the basis of preventive management. His first Edinburgh dispensary, opened in 1887, and its earliest London successor (1909) were as different from those "phthisical dispensaries" as a motor-car from a hackney coach. In his further historical peregrinations Dr. Hartston will no doubt run across more interesting institutions. But he is hardly likely to find a genuine tuberculosis dispensary before 1887.—We are, etc.,

G. LISSANT COX.

London, W.C.1. HARLEY WILLIAMS.

*** This correspondence is now closed.—ED., *B.M.J.*

Accidents from Gas Fires

SIR,—Dr. Allen Glenn's aged, sick, and rotund patient (*Journal*, March 29, p. 771) will be protected against the danger of fire, falling, and gas-poisoning if her gas fire is fitted with a bypass (and, of course, adequately guarded). The main tap can be placed anywhere in easy reach. I doubt if Dr. Glenn's ingenious suggestion of a thermostatically controlled tap is practicable.

At the other extreme of life, the meddlesome infant will be frustrated by the tap with a detachable key. In spite of its low cost, this device does not seem to be as well known as it deserves.—I am, etc.,

Chichester G. T. RUTHERFORD.

POINTS FROM LETTERS

Post-influenzal Depression

Dr. R. M. HARRISON (Orpington, Kent) writes: I was surprised to read Dr. L. A. Nichols's misconstrued reference (*Journal*, April 5, p. 833) to my letter "Post-influenzal Depression" (*Journal*, February 22, p. 460). My reference to alcoholic beverages was clearly made in order to dissociate them from methylpentynol carbamate ("oblivon-C").

Obituary

B. A. PEROTT, M.D., L.M.S.S.A., Arch.D.

Dr. B. A. Perott died suddenly on March 12 at the age of 75.

Born in St. Petersburg on October 26, 1882, Boris Andrew Perott completed his medical education at the Imperial Military Medical Academy there, and graduated M.D. in 1908. He then embarked upon a career of unusual versatility. Having already gained a diploma from the St. Petersburg Institute of Architects (for his studies into musical instruments) he spent some time in Finland as assistant lecturer in chest diseases at the Imperial Sanatorium in Halila. In 1919 he returned to Russia, but left almost immediately. He then came to London, and after further medical training obtained the L.M.S.S.A. in 1926. For nearly twelve years Dr. Perott served as a member of the editorial board of the *Tuberculosis Index* as abstracter in Russian. He was president of the Russian Medical Association of Great Britain. In Russia he had gained a reputation as a brilliant guitarist, and he founded the Philharmonic Society of Guitarists in London in 1929. He took a deep interest in the Boy Scout movement, and became an International Commissioner. Dr. Perott was familiar with no fewer than eighteen languages. With his death goes yet another link with the old Imperial Russia and its extraordinary range of cultural interests.—H. W.

C. K. J. VAUTIER, M.B., M.R.C.P., D.M.R.D., D.C.H.

Dr. C. K. J. Vautier, consultant radiologist to the Merthyr and Aberdare Hospital Group, died suddenly at his home at Merthyr Tydfil on March 30. He was 56 years of age.

Charles Keith John Vautier was born at Hastings, New Zealand, on October 20, 1901, son of an architect, and grandson of a pioneer who emigrated from Jersey almost a century ago. One of a family of six, he was educated at schools in New Zealand, and subsequently studied medicine at the medical school of the University of Otago, graduating M.B., Ch.B. from the University of New Zealand in 1928. After being a hospital resident for some years at Napier and Thames, he came to Great Britain in 1931, and practised widely in hospitals at various places, including Wembley, Carmarthen, Swansea, the Isle of Wight, Birmingham, Essex, and London. In 1941 he became a Member of the Royal College of Physicians of London, and in 1945 obtained the Diploma in Child Health of the English Royal Colleges and in 1951 the Diploma in Medical Radiodiagnosis. In 1949 he joined the department of radiology of the Postgraduate Medical School, Hammersmith, and was thereafter engaged in and around London until appointed consultant radiologist to the Merthyr and Aberdare Hospital Group in January, 1954. There he worked tirelessly in an expanding department, where heavy demands were made upon him, and his responsibilities were onerous. He none the less devoted much time to medical affairs concerning the hospitals, serving keenly on the group medical staff committee, and acting during the past twelve months as its secretary. His advice and help were at all times freely and most generously given to his colleagues, by whom his great and varied experience was valued very highly. In March, 1956, he married Miss Marguerite Rea, and established his home at Merthyr Tydfil only two years before his sudden and untimely death.

V. J. D. writes: Charles Vautier was widely travelled both in the Old World and in the New. He was a keen motorist and an ardent musician. A conscientious and selfless worker, he made a tremendous contribution to the care and welfare of the sick, but, above all, he was to many a generous-hearted and faithful friend, who in truth

thought far more of others than of himself. His passing is a tragic loss to the community and to a large circle of friends in all parts of Britain. He leaves two brothers and two sisters in New Zealand and a sister in Hollywood, California. To his devoted widow, who has above all suffered the grief of his loss, the deepest sympathy is extended.

JOHN MacLEOD, M.D.

Dr. John MacLeod, who had been in general practice in Fraserburgh for the last fifteen years, died suddenly on April 13, within two weeks of his 65th birthday.

John MacLeod was born in the island of Lewis on April 25, 1893. Throughout his school career he showed promise of distinction and was dux of the Nicolson Institute, Stornoway, in 1913. In that year he entered Aberdeen University as a medical student, but the first world war interrupted his studies. He immediately joined the Ross Mountain Battery of Artillery, and his 22nd birthday dawned for him with all the violence of war, as he was engaged in the first day of the attack on the Gallipoli peninsula. He returned to Aberdeen towards the end of the war and graduated M.B., Ch.B. in 1922. After holding the appointment of house-surgeon at the Royal Northern Infirmary, Inverness, he had his first experience of general practice as an assistant in the neighbourhood of Leeds. Moving to Ingleton, in the West Riding of Yorkshire, in 1926, he remained there for eight years. Then followed a period of nine years at Biggar, Lanarkshire. He finally settled at Fraserburgh in 1943.

J. M. writes: John MacLeod was a hard worker and a keen student of medicine. He set himself a high standard in all his endeavours. Perhaps his hardest and best work was done among the rural population of the Ingleton district of the West Riding, where, among many other activities, he was in charge of the antenatal and child welfare clinics. For his thesis on the problems of maternal mortality and morbidity and obstetrics in general practice he was granted the M.D. in 1935. At the time of his death he was physician to the Thomas Walker Hospital and medical officer to the Fraserburgh Maternity Hospital. A member of the British Medical Association for thirty-six years, he was also a foundation member of the College of General Practitioners. He was a family man, and at his best in the family circle. As husband, father, and host he excelled. All friends felt the warmth of his friendliness, kindness, and goodness, and will regret his passing. Sincere sympathy is extended to his wife, daughter, and four sons, one of whom is Dr. E. C. MacLeod.

D. A. GRATTAN, M.B., Ch.B.

Dr. D. A. Grattan died at his home at Mill Hill, London, on April 14 after a long illness. He was 59 years of age.

Donald Arthur Grattan was born on August 5, 1898, and entered the medical faculty of Sheffield University, after serving as a combatant officer in the West Yorkshire Regiment during the first world war. He obtained the M.B., Ch.B. degrees in 1924, and after holding resident appointments in medicine, surgery, and orthopaedics at the Sheffield Royal Hospital, and obtaining some experience of general practice, he settled in what was then the rapidly expanding district of Mill Hill, on the outskirts of London. There he built up a large practice, and that despite a serious illness, involving many operations, which kept him away from his patients for a year. The years of the second world war put a heavy strain upon him, and he was unable to work on account of another serious illness lasting for several months in 1943. Nothing daunted, he returned to the work which he loved, until his last illness struck him down in 1956. Such was his courage that in the summer of that year, when unable to use his right hand, and despite having had no previous tuition, he taught himself to paint pictures with his left hand. Besides his ordinary practice, Dr. Grattan was on the staff of the Hendon District Hospital for many years, and was also medical officer to John Groom's Crippleage at Edgware. A keen B.M.A. man, he held office as chairman of the Hendon Division in 1942, and he was a foundation member of the College of General Practitioners. He leaves a widow and one son, who is a veterinary surgeon.—A. C. P.

C. R. COWAN, M.B., B.S.

Dr. C. R. Cowan, who was in general practice at Ellesmere Port, Cheshire, died from poliomyelitis at Fazakerley Hospital, Liverpool, on April 16 after a few days' illness. He was 32 years of age.

Charles Robert Cowan was born at Ossett, Yorkshire, on February 17, 1926, and was educated at Worksop College, Nottinghamshire. He studied medicine at the London Hospital, and graduated M.B., B.S. from London University in 1949, taking the London Conjoint diploma in the same year. After graduation he became orthopaedic house-surgeon to Sir Reginald Watson-Jones at the London Hospital, and, after a period of six months, was appointed house-physician to Dr. J. R. B. Hern at St. Mary's Hospital, Portsmouth, for a further six months. He was then appointed surgical registrar at Bolton Royal Infirmary, where he remained for a period of two years. He joined the Royal Air Force as a medical officer in 1952, and served for a period of two years, being discharged in 1954. Since January 1, 1955, he had been in general practice in Ellesmere Port, first as an assistant, and, for the last two years, as partner with Dr. F. J. Jack, during which time he gained the esteem and affection of his colleagues and patients alike, and by his conscientious approach to his work upheld the highest standards of general practice in the district, where his loss will be greatly felt. He is survived by his wife and two children, to whom much sympathy is extended.—F. J. J.

LADY ALDEN, M.D.

Lady Alden died peacefully at Chappel, near Colchester, on April 24 at the age of 90.

Margaret Elizabeth Pearse was born in Madagascar on November 12, 1867, the daughter of the Rev. Joseph Pearse, and was educated at Walthamstow Hall, Sevenoaks, Kent, a school for the daughters of missionaries. She spent her holidays with an uncle, who was a doctor in the Highlands of Scotland, and it was while going with him on his rounds in the gig that she made up her mind to become a doctor herself. She studied medicine at Edinburgh and took the Scottish triple qualification in 1890, and then went to Berne, where, after learning German, she obtained the M.D. in 1892. Shortly afterwards she became a general practitioner in Canning Town, London, and was instrumental in starting the Balaam Street Hospital. In Canning Town she met and, in 1899, married Mr. (later Sir) Percy Alden, then warden of Mansfield House University Settlement and later Member of Parliament for Tottenham. Four daughters were born during the years 1900 to 1907. She resumed some medical work a year or two before the first world war, and, during the war, worked first with Belgian refugees at the Alexandra Palace, and later as doctor to a Belgian convent and school. For this work she received the Order of Queen Elizabeth. After the war she continued to work as medical officer at infant welfare centres in Stratford, Kentish Town, and Woking. Child welfare was a subject close to her heart, and as early as 1907 she had published a book entitled *Child Life and Labour*. In addition to her professional work she found time to help her husband in his political career and in his work as chairman of the Save the Children Fund. From the late 'twenties family matters claimed more of her time, although she still saw private patients and wrote for the medical press. She kept abreast

of new developments until she was well over 80. Soon after her husband's death in an air raid in 1944, she went to live in Essex with her youngest daughter, and spent the last years of her life in peaceful surroundings. One of her brothers is Dr. James Pearse.

F. B. MANSER, M.B., B.Chir.

Dr. F. B. Manser, honorary consulting surgeon to the Kent and Sussex Hospital, Tunbridge Wells, died at the hospital on April 28. He was 82 years of age.

Frederick Bailey Manser was born on December 19, 1875, the son of Dr. Frederick Manser, of Tunbridge Wells. Educated at Eastbourne College, Peterhouse, Cambridge, and Guy's Hospital, he qualified M.R.C.S., L.R.C.P. in 1901, taking the M.B., B.Chir. degrees two years later. After qualification he held a number of house appointments and then joined his father in practice in Tunbridge Wells. In 1914 he volunteered and served in the R.A.M.C. throughout the first world war. On resuming practice he was appointed to the staff of the Tunbridge Wells and Counties General Hospital as honorary surgeon in 1919, becoming senior surgeon in 1932. He was chairman of the Tunbridge Wells Division of the British Medical Association from 1934 to 1936. He is survived by his widow. There was one son, Robin, a soldier, who was killed in action with his regiment, The Queen's, early in 1940.

J. A. S. writes: In 1930 a great many improvements and alterations were needed, both at the Tunbridge Wells and Counties General Hospital and at the Royal Tunbridge Wells Eye and Ear Hospital, and Manser took a leading part in the courageous decision to scrap both and build a new hospital on the beautiful Culverden Park site. Through the years of planning, building, and raising money he worked hard, and it was a great joy to him when the Duchess of York—now Queen Elizabeth the Queen Mother—laid the foundation stone in 1932. The Kent and Sussex Hospital was completed and opened in 1934. Manser retired to the honorary consulting staff in 1935 but returned in 1940 to take over the post of hospital officer under the Emergency Medical Service. This post he held throughout the second world war, retiring again in 1946. He discharged the onerous duties with great administrative ability, tact, and kindliness. Many hundreds of Service men, evacuees, and local people came to know and love him well, and when he finally retired he was greatly missed, though scarcely a day passed without his frail but eager figure appearing in the hospital. He has left a gap in the lives of all who serve the hospital and all who knew him.

KHAN SAHIB, M.R.C.S., L.R.C.P.

Dr. Khan Sahib, former Chief Minister of West Pakistan and leader of the Republican Party, was assassinated on May 9 at Lahore. He was 76 years of age.

Khan Sahib was the son of a landowner in the Peshawar district and was educated at the Government High School and Mission College of Peshawar. He came to London in 1909 to study medicine at St. Thomas's Hospital, qualifying M.R.C.S., L.R.C.P. in 1917. His long friendship with Mr. Nehru began during their student days in London. Joining the Indian Medical Service immediately after qualification, he served in Mesopotamia and elsewhere during the first world war. Soon resigning his commission, however, he practised for the next few years among the Pathans of the North-West Frontier Province. His brother, Abdul Ghaffar Khan, had by this time become well known as leader of the "red shirt" movement, and Khan Sahib was also soon drawn into a turbulent political career. One of the most prominent of those who were struggling for Indian independence, he was first imprisoned in 1932. Later he became Prime Minister of the North-West Frontier Province, being leader of the Congress Party of the Assembly. During the second world war he was interned, resuming the premiership in 1945. After partition Khan Sahib was not regarded with favour by the Government of Pakistan, and for some years he was not at liberty to leave his own province. When, however, in 1954 a new Coalition Ministry was formed Dr. Khan became Minister of Communications. A year later he became the first Chief Minister of West Pakistan. He resigned from office last year.

Medical Notes in Parliament

TAX RELIEF FOR PROFESSIONAL SUBSCRIPTIONS

Mr. J. E. S. SIMON, Financial Secretary to the Treasury, moving the second reading of the Finance Bill on May 12, expanded a little on the proposal to give relief on professional subscriptions. The new provisions are contained in Clause 14 of the Bill. Mr. Simon referred to them as the outcome of the consideration, promised in the discussions on last year's Bill, to proposals for modifying the Schedule E expenses rule. Representations had been received, he said, from many associations and institutions, and the Chancellor had considered them carefully. The clause embodied a proposal which had received much support. Relief would be allowed for annual subscriptions to professional bodies and learned societies with activities related to the employee's work. Subscriptions to associations such as the medical defence associations, and the statutory registration fees paid by such people as architects and dentists as a condition of being allowed to practise, would also be allowed. The Inland Revenue Commissioners would approve societies, for the purpose of allowance of subscriptions, by reference to the criteria laid down in the clause, and subject, of course, to the usual rights of appeal, and the general test would be whether a society's activities were wholly or mainly of a professional or learned character. Where such a body also had significant activities of a different kind, such as the prosecution of salary claims, the clause provided for deduction of a fairly apportioned part of the subscription.

ANSWERS TO QUESTIONS

More Vaccine from America

Mr. R. FORT (Clitheroe, Con.) asked the Minister of Health on May 12 when the substantial new supplies of Salk vaccine would become available for use in this country. Mr. WALKER-SMITH informed him that two million doses of Salk vaccine which had passed their tests and been licensed for issue in America were due to arrive on May 13, and they would be distributed immediately to local health authorities. Another one and a half million doses of this vaccine were expected the following week. In addition a batch of half a million doses of British-tested Salk vaccine was now being distributed, and further supplies were expected as tests were completed.

Mr. FORT asked what was the estimated percentage of those expected to be registered by the end of July who would remain unvaccinated when these and subsequent lots had been distributed. Mr. WALKER-SMITH told him that with these supplies the vaccination programme could be kept going at full speed. A precise answer must depend on the number of late registrations. Mr. M. EDELMAN (Coventry, North, Lab.) asked if the Minister would give an assurance that Salk vaccine could be used in full confidence. Mr. WALKER-SMITH stated that a circular had been issued to medical officers, and detailed guidance, including the M.R.C. report, had been sent to them. He did not think he ought to put a gloss on the expert guidance which had been given to the doctors, to whom parents should turn for individual advice.

Progress with Vaccination

Mr. EDELMAN asked what percentage of those eligible for immunization against poliomyelitis were either unvaccinated

or had received only one inoculation against poliomyelitis at the latest date for which these figures were available. Mr. WALKER-SMITH stated that in Great Britain at the end of February, the latest date for which national figures were available, 52% of those in the eligible groups who had registered were awaiting vaccination and 11% had had only one injection. Figures for the end of April should become available in a day or two.

Mr. EDELMAN suggested that the figures reflected the anxiety of parents because imported vaccine had been given second or third place, and asked if the Minister would positively recommend Salk vaccine. Mr. WALKER-SMITH said he did not think the registration figures necessarily reflected that. In any event the figures were for February, and no doubt the April figures would show a material increase in registrations. In the United States there were still one in four out of 65 million persons under 20 not yet vaccinated, and 40% of all children under 5 had not begun their vaccination.

British Production

Mrs. BARBARA CASTLE (Blackburn, Lab.) asked the Minister what target he had set for the production of anti-poliomyelitis vaccine by Messrs. Glaxo and Burroughs Wellcome, respectively. Mr. EDELMAN asked him what invitations he had given to firms other than the present contractors to participate in the production of the British type of anti-poliomyelitis vaccine. Mr. WALKER-SMITH replied that it continued to be the Government's intention that as soon as supplies were sufficient only the British type of vaccine should be used in the vaccination scheme. The manufacturers were aware of this, and the issue of individual invitations to produce vaccine did not arise. Nor was there any question of the Government setting a production target for individual firms.

Mrs. CASTLE said that on a recent television programme Dr. Wheeler, of Burroughs Wellcome, explained that his firm had had no kind of guidance from the Ministry on how much they should produce, and they had set their own target of nearly four million doses a year. As this was inadequate to meet current needs, was it not nonsense to talk about making the British vaccine the basis of our supplies? Was it not wrong to leave the production of British vaccine purely to the initiative of individual firms, governed by commercial considerations, as Dr. Wheeler made clear?

Mr. WALKER-SMITH.—I am not responsible for what is said on A.T.V. programmes. The orders placed with the British manufacturers were the quantities which the firms thought they could produce for six months. The quantities delivered did not come up to the orders placed, so I do not think it can be said that the Government were remiss in not placing larger orders.

Mr. EDELMAN.—But since the Minister has described this as the "safest" vaccine, and said it is his ultimate aim to provide it for all children to be vaccinated, why does he tolerate a semi-monopoly of this vaccine? Why does he not invite the whole pharmaceutical industry to co-operate in producing the vaccine, which should be made available to every child?

Mr. WALKER-SMITH.—It is not a matter of the Government issuing invitations to these commercial companies to produce this vaccine. Only large and well-equipped companies can enter into this. I would welcome supplies of British vaccine which is up to standard from any source, and I am certainly ready to consider the purchase of British-type vaccine from whichever company chooses to put it forward.

Dr. EDITH SUMMERSKILL (Warrington, Lab.).—Has the Minister told the companies, other than Messrs. Glaxo and Burroughs Wellcome, that he is prepared to receive it?

Mr. WALKER-SMITH.—I think they are well aware of that, and there is a third British firm which has entered into production.* He added that he had not specifically asked only Messrs. Glaxo and Burroughs Wellcome to produce the vaccine. Orders were placed with them because they were the only two firms which were able to accept orders and to promise deliveries. If the third company's vaccine passed the M.R.C. tests, he was fully prepared to consider placing orders with them.

*We understand that the third firm is Messrs. Pfizer Ltd., of Folkestone.

Hospital Private Beds

Mr. JOHN HALL (Wycombe, Con.) asked the Minister of Health on May 5 if he would abolish hospital private beds and replace them by the same or greater number of amenity beds. Mr. D. WALKER-SMITH replied "No."

Mr. HALL said that the demand for amenity beds by those to whom privacy was essential for speedy recovery was far greater than the number available. As a result they were being forced into private beds at great and sometimes extortionate cost. Would the Minister reconsider this decision? Mr. WALKER-SMITH said that he was always prepared to consider proposals for private or amenity beds where this was possible and where, in the view of the regional hospital board, there was a demand. But he pointed out that there was still a demand for private treatment, and it would not be appropriate to go back on the decision that the House took in 1946.

Medicines for Private Patients

Lieutenant-Colonel W. BROMLEY-DAVENPORT (Knutsford, Con.) asked the Minister whether, when his discussions with the British Medical Association were finished, he would issue a statement; and whether, during his negotiations, he would ask the Association for an estimate of the average weekly number of private patients who receive medicines or drugs. Mr. WALKER-SMITH said the answer to both parts of the question was "Yes," but he was not yet able to say when the discussions would be completed.

Lieutenant-Colonel BROMLEY-DAVENPORT said it was extremely unfair that private patients who were forced to contribute to the Health Service should have to pay for their drugs and medicines. This was the kind of vindictive Socialist legislation which the country expected the Conservative Party to put right. Mr. WALKER-SMITH replied that he had indicated previously that the Government were not unmindful of the principle that he had in mind, but that it would not be possible at present to introduce legislation which would result in increased expenditure.

Bacterial Rodenticides

Mr. ROBERT JENKINS (Dulwich, Con.) asked the Minister of Agriculture, Fisheries, and Food whether, having regard to the recommendations about the use of bacterial rodenticides by the Working Party on Toxic Chemicals in Agriculture (Residues in Food), he would make a statement.

Mr. JOHN HARE said he had been informed by the company that was using this method that since May 1 it had discontinued the use of bacterial rodenticides in the United Kingdom and would not resume their use without his approval.

Crimes of Violence and Murder

Sir THOMAS MOORE (Ayr, Con.) asked the Secretary of State for the Home Department on May 8 for any information he could give the House about his intentions regarding a revision of the Criminal Justice Act, 1948, and the Homicide Act, 1957.

Mr. R. A. BUTLER said that the report of the study of the Cambridge Department of Criminal Science on crimes of violence in the Metropolis, to which he assumed Sir Thomas Moore was referring, was not yet available. As to the Homicide Act, he was glad to say that the monthly figures for murders recorded as known to the police in England and Wales in the six months September, 1957, to March, 1958, had been considerably lower than those for the months immediately after the passing of the Homicide Act. The total for the six months was 92, which was slightly lower than the figure for the corresponding period in 1954–5. He would continue to watch the situation closely, but experience so far did not suggest a need for amending legislation.

"Guard That Fire"

Mr. R. A. BUTLER, replying to Mrs. MCLAUGHLIN (Belfast, West, U.U.), said he shared her concern at the extent of burning accidents caused by clothing in contact with unguarded fires. He believed that the biggest single contribution to its solution lay in persuading householders and other responsible persons to provide and use efficient fireguards. A "Guard that Fire" campaign was to be launched next November. Circulars had been sent to local authorities inviting them to co-operate by organizing local campaigns on this theme.

London Teaching Hospitals

Mr. M. LIPTON asked the Minister of Health on May 12 what plans he was considering to reduce or change the number of London teaching hospitals. Mr. WALKER-SMITH.—None. Mr. LIPTON asked the Minister if he had seen reports that he was considering closing three London teaching hospitals—Charing Cross, Westminster, and St. George's. Was there any truth in the report? Mr. WALKER-SMITH replied that he had seen the report, which was in a usually reliable newspaper, but he was not considering that course. There were certain processes in mind with regard to Charing Cross Hospital and the Royal Free Hospital, but there was no question of amalgamation.

Merit Awards

Mrs. LENA JEGER (Holborn and St. Pancras, South, Lab.) asked the Minister why the identity of consultants who received merit awards was kept secret; and whether he would consider the abolition of the present system. Mr. WALKER-SMITH stated that the balance of advantage was against the general publication of the identity of the consultants in question. The Government's views on the merit award system itself had been given in evidence submitted to the Royal Commission on doctors' and dentists' remuneration, and it would be more appropriate if he deferred further comment until the Royal Commission's report was received.

Artificial Limbs

Mr. C. J. SIMMONS (Brierley Hill, Lab.) asked the Minister to indicate the steps being taken to develop the work of the department of research and experiment to secure improvements in the design, performance, and fitting of artificial limbs; and the extent of any co-operation which existed to secure precise information about new artificial limbs and appliances available in other countries. Mr. RICHARD THOMPSON, Parliamentary Secretary, Ministry of Health, stated that since last year the work of the research department at Roehampton had been under the regular supervision of a small executive committee of the Standing Advisory Committee on Artificial Limbs. On the recommendation of these committees a special plastics laboratory was about to be established. The research staff kept in close touch with colleagues in other countries by correspondence, exchange of literature and samples, and by visits. Two members of the staff were at present visiting research establishments in the United States.

Universities and Colleges

UNIVERSITY OF OXFORD

The following have been reappointed University Demonstrators, in the subjects indicated in parentheses, from October 1, 1958, to September 30, 1963: Dr. J. E. French (Pathology); Mr. T. P. S. Powell (Human Anatomy); and Dr. G. Gordon (Physiology).

UNIVERSITY OF CAMBRIDGE

In Congregation on March 8 and 10 the following degrees were conferred:

M.D.—M. H. S. Bound, K. J. Martin, P. E. Hughesdon, P. J. Crowley.
M.CHIR.—R. G. Beard.
M.B., B.CHIR.—*By proxy*: D. S. Filer.
M.B.—J. G. Miller, C. S. Goodwin.

Medico-Legal

HYPERTHERMIA IN THE NEWBORN

FAILURE OF AN INCUBATOR

[FROM A PAEDIATRIC CORRESPONDENT]

A premature baby weighing 4 lb. 2 oz. (1.87 kg.) at his birth on December 1, 1957, was being cared for in an incubator. He had had a few septic spots which were healing, and a number of loose motions containing blood. At 8 p.m. on December 11 a nurse noticed that he was rather warm, and the lid of the incubator was therefore raised. At about 9 p.m. the baby was noted to have mucus round his mouth and his head was lowered, but at 9.45 p.m., as his condition did not appear satisfactory, the incubator lid was closed so that oxygen could be given. At about 10 p.m. the incubator temperature was found to be 105° F. (40.6° C.) and the baby's rectal temperature 106° F. (41.1° C.). The baby seemed to have recovered during the next few hours, but died next morning.

Post-mortem examination showed a male child, weighing under 4 lb. (1.8 kg.), with "a trace of old intraventricular and subarachnoid haemorrhage" in the brain, patchy pulmonary collapse and pleural petechiae, and dilatation of all the chambers of the heart. There was intense congestion of the jejunum and evidence of acute enteritis. The kidneys, ureters, and adrenals were markedly congested. The incubator concerned was found to have the thermostat set at the maximum position of ten. Testing showed a faulty electrical connexion causing a heater under the thermostat not to function properly, and a failure of the excess temperature cut-out to operate at the correct temperature of 105° F. (40.6° C.). The audible warning system, which gives a signal when the temperature rises above this temperature, was not fitted to this incubator.

A coroner's jury concluded that death in this case was due to acute infective enterocolitis, prematurity, and subarachnoid birth haemorrhage. Whether the incubator played any part was uncertain.

Comment

A case such as this raises the question of the diagnosis of hyperthermia in the newborn. The usual symptoms of overheating are fairly well known and are similar in both the premature and the full-term infant. Most commonly they are seen in a baby who has been over-zealously wrapped up and kept in a warm room to prevent chilling, but they are also encountered for the same reasons in the pyrexial or ill baby who has to be transported by ambulance to hospital. There is generalized bright-red erythema, respirations and pulse are very rapid, and the baby may be restless. Sweating is absent in the premature, and absent or almost unnoticeable in the full-term child. Continued hyperpyrexia, as in an incubator failure, leads to cerebral signs—contraction of the pupils, twitching, fits, increased cerebrospinal fluid pressure—and death. Woodruff[1] states that at necropsy there is invariably congestion of the internal organs and petechial haemorrhages in the lungs, gastro-intestinal tract, and viscera. The meninges are congested and subarachnoid haemorrhages are present.

Newborn babies, and premature ones in particular, are more susceptible to sudden changes in temperature than older children, and their inability, or relative inability, to sweat renders them particularly sensitive to high temperatures. The scientific literature as distinct from the anecdotal is very scanty on this subject, and there seems no reliable evidence on the degree or duration of fever an infant can stand without coming to harm.

REFERENCE

[1] Woodruff, A. W., *Paediatrics for the Practitioner. Supplement*, 1956, p. 90. Butterworth and Co., London.

HUSBAND'S FEMININE BEHAVIOUR CRUELTY

[FROM OUR LEGAL CORRESPONDENT]

On March 14 in the High Court Mr. Justice Collingwood granted a decree of divorce to Mrs. Meta Gertrude Williams, of St. German's Road, Forest Hill, S.E., on the ground of her husband's cruelty (*The Times*, March 15).

The parties were married in 1947, and the trouble between them started in August, 1952, when Mr. Williams read in the newspapers about an operation on an American airman in Denmark by which his sex was said to have been changed. He then told his wife that since boyhood he had wanted to be a woman, that he prayed every night that he would awake to find that he was one, and that they should live thenceforward as brother and sister.

In September, 1955, after Mr. Williams had started dressing up as a woman, Mrs. Williams in the course of a serious talk with him told him it was upsetting her very much and she could bear it no longer. He said he loved dressing up in that way and gave her a shocking account of an incident in Brighton where there was a man who made women's clothes for him, and Mrs. Williams was terribly distressed and revolted and said she would never be a wife to him again. After this he took to wearing women's clothes most evenings and women's underwear during the day, and from Christmas, 1955, his main topic of conversation was what would happen when he had saved enough money to have an operation to change him into a woman. In June, 1956, there was a series of incidents while Mrs. Williams's parents were visiting them, culminating with Mr. Williams appearing before them dressed as a woman. On this, Mrs. Williams left him.

In his judgment the judge said that he did not accept Mr. Williams's case that he had only dressed up as a woman on four or five festive occasions as a joke. The wife's evidence was supported by independent witnesses and the production of an order form for a woman's wig costing £17–£20 filled in in his writing. He had persisted in a long course of conduct in spite of the distress which he knew it caused to his wife. Since he had intentionally pursued a course of conduct which he must have known would ultimately have a serious effect on her health, that amounted to cruelty, and Mrs. Williams must be granted a decree.

Vital Statistics

Eire in 1957

The provisional summary for Eire in 1957 shows that the birth rate was 21.2 per 1,000 population and was 0.2 above the rate for 1956. The infant mortality rate was 33 per 1,000 registered births; this rate was 3 below the rate for 1956. The death rate was 11.9 per 1,000 population, being 0.2 above the rate for 1956. Deaths from respiratory tuberculosis numbered 584 and from other forms 113, the former being 22 more and the latter 14 fewer than in 1956. Deaths from malignant neoplasms numbered 4,817, of which 1,026 were of the stomach, 1,311 of the digestive organs and peritoneum, and 622 of the respiratory system. Deaths from infectious diseases included 687 from influenza, 20 from whooping-cough, 19 from measles, 13 from acute poliomyelitis, and 6 from diphtheria.

The birth rate for the December quarter of 1957 was 20.4 per 1,000 population, being 0.1 above the rate for the preceding fourth quarter. The infant mortality rate was 33 per 1,000 registered births, which was 2 below the rate for the corresponding quarter of 1956. The death rate was 12.6 per 1,000 population and 1.7 above the rate for the 1956 quarter. The 489 deaths from influenza were the largest number recorded since the first quarter of 1951. The numbers of deaths attributed to tuberculosis were 164 from respiratory and 23 from other forms, and were 41 and 3, respectively, more than in the preceding fourth quarter.

Scotland in 1957

The preliminary returns for Scotland in 1957, supplementing earlier figures (*Journal*, April 12, p. 897), gave a birth rate of 19.0 per 1,000 population, the highest since 1948. The infant mortality rate was 29 per 1,000 living births and was the same as the rate for 1956. The death rate was 11.9 per 1,000 population and was 0.1 below the rate for 1956 but the same as the average for the five preceding years. The number of deaths from the principal epidemic diseases was 741, being 422 more than in 1956. These deaths included 681 from influenza, 21 from whooping-cough, 21 from meningococcal infections, 16 from measles, 11 from acute poliomyelitis, and 2 from scarlet fever. 664 deaths were attributed to respiratory tuberculosis and 59 to other forms of tuberculosis, being 51 and 27, respectively, below the totals for 1956. Deaths due to violence numbered 2,800, or 158 more than in 1956. Of these deaths 412 were suicides, 584 due to road transport accidents, and 1,804 to other forms of violence; the numbers were 9 more, 4 fewer, and 153 more, respectively, than in 1956.

In the fourth quarter of 1957 the birth rate was 18.6 per 1,000 population and was 1.3 above the average of the five preceding fourth quarters. The infant mortality rate was 29 per 1,000 registered live births, 1 below the rate for the preceding fourth quarter; the neonatal mortality rate was 20, the same as the rate in the corresponding quarter of 1956. The death rate was 13.1 per 1,000 population and was 1.4 above the five years' average. There were 550 deaths from the principal epidemic diseases—519 more than in the fourth quarter of 1956. This large rise was due to influenza, with 539 deaths. Deaths from respiratory tuberculosis numbered 207 and deaths from other forms of tuberculosis numbered 19. The deaths from respiratory tuberculosis were 31 more and the deaths from other forms were 4 fewer than in the corresponding quarter of 1956.

Week Ending May 3

The chief fluctuations in the notifications of infectious diseases in England and Wales during the week ending May 3 were decreases of 217 for measles, from 3,916 to 3,699, 111 for dysentery, from 927 to 816, 82 for acute pneumonia, from 507 to 425, and increases of 128 for scarlet fever, from 628 to 756, 30 for food-poisoning, from 146 to 176, and 23 for whooping-cough, from 655 to 678.

A general fall in the incidence of measles was recorded; the largest decrease in the number of notifications was 82 in Kent, from 165 to 83. A small rise in the incidence of scarlet fever occurred in most regions of the country, but there were no large changes in the local trends. The largest rise in the number of notifications of whooping-cough was 34 in Yorkshire West Riding, from 36 to 70. The notifications of diphtheria numbered 3, being the same number as in the preceding week.

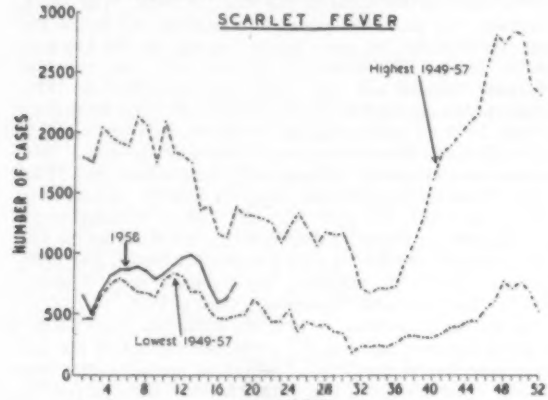
The number of notifications of acute poliomyelitis was 20, there being 2 fewer for paralytic and 1 more for non-paralytic cases than in the preceding week. The largest returns were London 4 and Yorkshire West Riding 3.

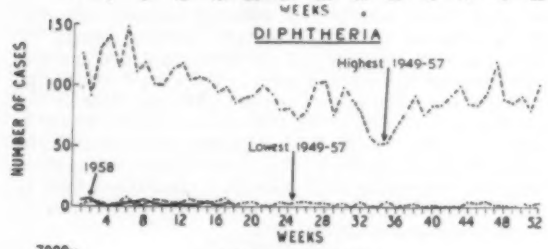
The chief centres of dysentery were Lancashire 224 (Liverpool C.B. 55, Manchester C.B. 44, Oldham C.B. 31, Kirkby U.D. 10, Worsley U.D. 10), Yorkshire West Riding 175 (Sheffield C.B. 28, Leeds C.B. 20, Pontefract M.B. 17, Bradford C.B. 11, Huddersfield C.B. 11), London 100 (Islington 22, Hackney 18, Lewisham 11), Gloucestershire 61 (Bristol C.B. 50), Cheshire 32 (Northwich R.D. 12), Durham 21, Surrey 28 (Godstone R.D. 26), Warwickshire 24 (Birmingham C.B. 16), and Staffordshire 23.

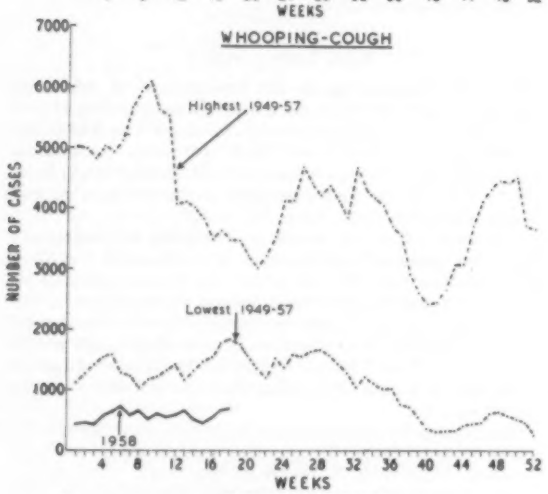
The largest outbreaks of food-poisoning during the week were 23 in Bolton C.B., 21 in Liverpool C.B., and 20 in Edmonton M.B.

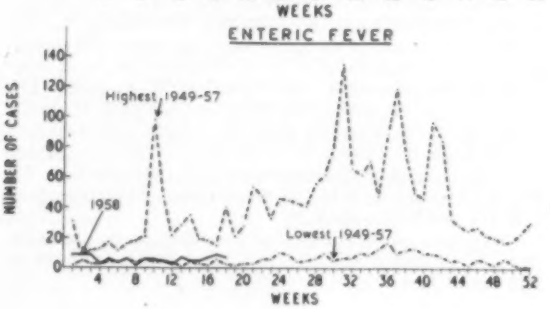
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus ------, the figures for 1958 thus ———. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **April 26** (No. 17) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire	1957 Eng. & Wales	1957 Lond.	1957 Scot.	1957 N. Ire.	1957 Eire
Diphtheria ..	3	1	3	0		7	0	2	0	1
Dysentery ..	927	78	175	3	1	570	26	323	13	5
Encephalitis, acute	3	0		0		2	0		0	
Enteric fever:										
Typhoid ..	6	0	0	0	1	5	0	0	1	
Paratyphoid ..	3	0	5(B)	0	4(B)	2	0	4(B)	0	
Food-poisoning ..	146	26	10	4		134	12	14	1	
Infective enteritis or diarrhoea under 2 years				10	20				11	25
Measles *	3,916	294	147	47	10	26,960	1780	213	376	339
Meningococcal infection	17	3	10	4	1	35	2	12	3	2
Ophthalmia neonatorum	26	0	9	0		21	0	5	0	
Pneumonia† ..	507	34	225	21	7	425	22	171	9	1
Poliomyelitis, acute:										
Paralytic ..	13	2	0	0	6	44	5	4	0	5
Non-paralytic	8	0				19	2			
Puerperal fever§ ..	211	34	5	3	1	248	42	8	1	1
Scarlet fever ..	628	44	83	30	19	542	30	65	39	16
Tuberculosis:										
Respiratory ..	608	73	135	16		570	81	371	23	
Non-respiratory	93	9	25	3		68	5	14	3	
Whooping-cough ..	655	28	55	16	9	2,237	84	236	7	59

DEATHS	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire	1957 Eng. & Wales	1957 Lond.	1957 Scot.	1957 N. Ire.	1957 Eire
Diphtheria ..	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery ..	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	10	0	0	0	0		1	0	2	0
Influenza	35	0	4	0	0		0	1	0	0
Measles		0	0	0	0		0	0	0	1
Meningococcal infection		0	0				0	1		
Pneumonia ..	654	50	23	13	11		40	18	14	9
Poliomyelitis, acute	3	0		0	0		2			0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	85	3	4	0	6		10	5	2	5
Non-respiratory		2	0	0	1		0	1	1	0
Whooping-cough ..	0	0	0	0	0		0	0	0	0
Deaths 0–1 year ..	327	29	33	5	12		27	15	11	16
Deaths (excluding stillbirths) ..	10,647	772	607	110	185		781	583	123	193
LIVE BIRTHS ..	14,456	1190	1160	248	416		1160	1122	206	424
STILLBIRTHS ..	321	24	28				24	24		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Empire Rheumatism Council.—Dr. W. S. C. COPEMAN, the Council's chairman, presented the Council's 21st report at the annual meeting in London on May 7. In his introduction to the report he announced definite progress in the Council's 10-year programme of intensified research and with last year's Birthday Appeal for £250,000. They still needed urgently £175,000, but with the funds already collected they had been able to endow for 10 years a second chair of rheumatology (at the Postgraduate Medical School of London, the other being at Manchester), and to support research on the aetiology of various rheumatic conditions. Surveys by the Council's mobile unit in the North of England, states the report, suggest that there may be two varieties of rheumatoid arthritis, one hereditary and the other not, and also that multiple osteoarthritis has a definite familial tendency; another result from the unit's surveys of random population samples has been the definition of rheumatoid arthritis of the cervical spine. Two of the Council's research fellows have completed their studies: Dr. J. K. NORYMBERSKI at Sheffield has for the last five years been studying the biochemistry of the adrenal steroids and their relationship to rheumatic diseases, while Miss I. H. M. MUIR, at St. Mary's Hospital, London, has been investigating the physical properties of the supporting tissues of the body. Ordinary income for the year ended October 31, 1957, was £33,913. The Council's offices are at Faraday House, 8–10, Charing Cross Road, London, W.C.2.

Medical Research in Scotland.—The Secretary of State for Scotland has appointed five new members to the Advisory Committee on Medical Research in Scotland. They are: Professor DUGALD BAIRD (Aberdeen), Professor D. M. DOUGLAS (St. Andrews), Professor T. FERGUSON RODGER (Glasgow), Professor E. J. WAYNE (Glasgow), and Dr. D. J. FINNEY, F.R.S. (Aberdeen). The committee, whose chairman is Sir ANDREW DAVIDSON, advises the Secretary of State on the initiation, direction, and conduct of medical research in Scotland, and also acts as the advisory body to the Scottish Hospitals Endowments Research Trust.

F.R.C.S.Ed.—At a meeting of the Royal College of Surgeons of Edinburgh on May 9 the following were admitted fellows:

E. G. Ahern, R. M. Anderson, M. S. Bansel, J. S. Greene Blair, P. S. Boulter, M. C. Desai, W. M. Hefni, T. V. Hingorani, E. A. Ingram, H. Jackson, M. M. A. Kader, B. H. Kelham, J. R. Kirkpatrick, P. Lebon, W. W. J. Liddle, W. A. A. G. Macbeth, G. B. McKelvie, M. R. Morris, D. A. O'Rourke, L. S. Parker, B. C. Paton, G. G. Powell, G. L. Ritchie, J. W. Rodwell, J. B. van Schalkwyk, B. P. Scrivener, S. J. Seevaratnam, M. M. Sinclair, K. Singh, L. Souvlis, N. W. Struthers, J. D. Thompson, J. C. Usdin, G. A. Whitefield, D. B. B. Whitehouse, W. W. Wilson, C. I. Woolf, and M. K. A. Youssef.

Experimental Research on Ageing.—The Trustees of the Ciba Foundation invite applications for their fifth and final annual awards for research relevant to basic problems of ageing. Not less than five awards, of an average value of £300 each, are available for 1959. Papers may be in the candidate's own language, but must not exceed 7,000 words in length and must be accompanied by a summary in English. Preference will be given to younger workers. Further details may be obtained from Dr. G. E. W. WOLSTENHOLME, Ciba Foundation, 41, Portland Place, London, W.1. The closing date for entries is January 10, 1959.

Postgraduate Study in Germany.—The German Academic Exchange Service offers a number of grants to foreign doctors for study at German university institutes and clinics. The grants are intended for younger members of the profession and are tenable for periods of up to twelve months. Their value is 425 DM. a month. The closing date for grants tenable from October next is May 20. Interested doctors should apply at once for further details and application forms to Herr G. MÜLLER, German Academic Exchange Service, 43, Parliament Street, London, S.W.1 (tel.: Whitehall 6879).

Birmingham University.—A special degree Congregation will be held on July 17 during the annual meeting of the B.M.A., at which the following honorary degrees will be conferred: LL.D. on Sir ALEXANDER DRUMMOND, Director-General, Army Medical Services; D.Sc. on Professor J. S. MITCHELL, F.R.S., Regius professor of physic at Cambridge; and M.D. on Dr. I. D. GRANT, president of the College of General Practitioners.

Assistant Secretary of the B.M.A.—The Council of the British Medical Association has decided to vary the terms of the advertisement of this appointment, details of which will be found in our advertisement columns (p. 32). No age limit is now stated, but preferential consideration will be given to candidates not over the age of 40.

New Member of W.H.O.—The Federation of Malaya, which recently became a member of the United Nations, has now joined the World Health Organization. W.H.O. now has 85 full members (including Malaya) and three associate members.

U.S. Secretary of Health.—The president of Ohio Wesleyan University, Dr. ARTHUR FLEMMING, is shortly to succeed the present U.S. Secretary of Health, Education, and Welfare, Mr. MARION FOLSOM, who is resigning. Dr. Flemming was previously director of defence mobilization.

Hunterian Society.—The gold medal for the Hunterian Society's essay competition for 1957 has been awarded to Dr. C. A. H. WATTS, of Ibstock, Leicester. The subject for the 1958 essay is "Impotence." The competition is open to all general practitioners. Further details may be obtained from the hon. secretary, Dr. C. W. KESSON, 51, Harley Street, London, W.1.

N.A.P.T. Canadian Scholarship.—Dr. P. D. B. DAVIES, consultant physician to the St. Pancras Chest Clinic, has been awarded this year's scholarship for three months' postgraduate study in Canada by the National Association for the Prevention of Tuberculosis. The return Canadian scholar is Dr. H. S. COULTHARD, of the Toronto Hospital for Tuberculosis.

Central Council for Health Education.—Dr. JOHN BURTON has resigned from the medical directorship of the Central Council for Health Education. Dr. A. J. DALZELL-WARD, deputy medical director since 1952, will succeed him on July 5.

Board of Registration of Medical Auxiliaries.—Dr. H. SEAWARD MORLEY and Mr. JOHN H. HANBY, immediate past-president of the Society of Chiropodists, have been appointed to the board's council.

Sir Russell Brain has had conferred on him the honorary fellowship of the Royal College of Surgeons of England.

Dr. P. M. B. Walker, of the Medical Research Council's biophysics research unit, has been appointed to a Royal Society research fellowship.

COMING EVENTS

Harben Lectures.—Professor A. BRADFORD HILL, F.R.S., will deliver three Harben lectures at the Royal Institute of Public Health and Hygiene on "The Experimental Approach in Preventive Medicine," at 5 p.m., on May 19 ("Problems of Experiments in Man"), May 20 ("Controlled Trials of Vaccines"), and May 21 ("Influenza and the Common Cold").

Croonian Lecture.—Professor P. B. MEDAWAR, F.R.S., will lecture at the Royal Society on "Homograft Reaction" on May 22 at 4.30 p.m.

Huxley Lecture.—Sir HOWARD FLOREY, F.R.S., will lecture at Charing Cross Hospital Medical School, at 5.30 p.m. on

May 22. His subject will be "The Changing Emphasis in Medical Research." Tickets (free) from the Dean of the School.

Société Française de Médecine Psychosomatique.—Meeting May 31 and June 1 in Paris. Details from Dr. L. CHERTOK, 22, rue Legendre, Paris, 17e.

Babinski Centenary.—La Société Française de Neurologie at its Réunion Neurologique Internationale in Paris will celebrate on June 2 the centenary of the birth of J. Babinski. The speakers will be Professor RAYMOND GARCIN, Sir FRANCIS WALSHE, F.R.S., and Dr. AUGUSTE TOURNAY. The two ensuing days of the meeting will be devoted to a symposium on the cerebellum.

Institute of Cardiology.—Dr. HOWARD BURCHELL, of the Mayo Clinic, U.S.A., will deliver the St. Cyres lecture at the Royal Society of Medicine on June 4 at 5 p.m. His subject will be "Studies of Pulmonary Hypertension in Congenital Heart Disease."

Second Ciba Foundation Lecture.—Professor Dr. F. BOURLIÈRE, of Paris, will lecture at the Royal Institution, London, on June 19 at 5 p.m. on "The Comparative Study of Age Changes." Tickets (free) from the Ciba Foundation, 41, Portland Place, London, W.1.

Anaesthetics for the G.P.—Two-weeks course in anaesthetics for general practitioners, from June 23, at the Postgraduate Medical School of London. Further details on p. 57 of the advertisements.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Archives of Disease in Childhood.—Issued six times a year (£4 4s. annually). The new issue (Vol. 33, No. 168) includes:

REGIONAL OBSTRUCTIVE EMPHYSEMA IN INFANCY. James Thomson and John O. Forfar.
AN INBORN ERROR OF METABOLISM WITH THE URINARY EXCRETION OF α-HYDROXY-BUTYRIC ACID AND PHENYLPYRUVIC ACID. Alan J. Smith and Leonard B. Strang.
A CASE OF HARTNUP DISEASE. Walter Henderson.
DISSOCIATION AS A GUIDE TO DEVELOPMENTAL ASSESSMENT. R. S. Illingworth.
DYSMATURITY. S. Sjöstedt, G. Engleson, and G. Rooth.
CONGENITAL INTERRUPTION OF THE AORTIC ARCH. Bridget V. Foley.
NORMAL DIAMETER OF THE HEART IN RADIOGRAPHS OF PRE-SCHOOL CHILDREN. David Hewitt.
THE CHANGING AETIOLOGY OF ERYTHEMA NODOSUM IN CHILDREN. John Lorber.
CLINICAL AND BIOCHEMICAL CHANGES DURING EXCHANGE TRANSFUSION. James W. Farquhar and Hylton Smith.
TREATMENT OF PERSISTENT ENURESIS WITH THE ELECTRIC BUZZER. Ian G. Wickes.
RECURRENT ABDOMINAL PAINS: A FIELD SURVEY OF 1,000 SCHOOL CHILDREN. John Apley and Nora Naish.
SALMONELLA MENINGITIS. Kenneth C. Watson.
CALCIFIED MESENTERIC LYMPHANGIOMA. R. L. Bishton, C. P. Sames, and Hugh R. E. Wallis.
SWEAT TEST FOR THE DIAGNOSIS OF FIBROCYSTIC DISEASE OF THE PANCREAS. K. A. Misch and H. M. Holden.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, May 19

MANCHESTER MEDICAL SOCIETY: SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre, Manchester University, 8.30 for 9 p.m., Presidential Address by Dr. C. Vipont Brown: All Change.
MARLBOROUGH DAY HOSPITAL.—8.15 p.m., Dr. E. M. Bluestone (New York): Social Psychiatry—A Critique.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. F. R. Keating: Diagnosis of Hyperparathyroidism.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—5 p.m., Harben Lecture by Professor A. Bradford Hill, F.R.S.: Experimental Approach in Preventive Medicine—Problems of Experiments in Man (illustrated).
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY.—5 p.m., Almroth Wright Lecture by Dr. R. G. White: Cellular Aspects of the Immune Response.

Tuesday, May 20

BRITISH ASSOCIATION OF SPORT AND MEDICINE.—At Middlesex Hospital Medical School, W., 5.30 p.m., Mr. A. E. H. Kendall: Athletes and Adaptation to Stress.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Miss Phyllis Wade: Radiation (Cancer II).
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Professor J. L. Wright (Otago): Modern Management of Placenta Praevia.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—5 p.m., Harben Lecture by Professor A. Bradford Hill, F.R.S.: Experimental Approach in Preventive Medicine—Controlled Trials of Vaccines (illustrated).

Wednesday, May 21

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Miss Christine Hodges: Radiation (Superficial).
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: Unilateral and Localized Emphysema of the Lung.
MANCHESTER MEDICAL SOCIETY: SECTION OF PATHOLOGY.—At Large Anatomy Theatre, Manchester University, 4 for 4.30 p.m., Dr. J. E. Kench: Aminoaciduria.
MEDICAL RESEARCH COUNCIL.—At National Institute for Medical Research, Mill Hill, N.W., 5 p.m., Professor J. Waldenström (Sweden): The Porphyrias.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. D. G. Evans: Immunization Against Poliomyelitis.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—5 p.m., Harben Lecture by Professor A. Bradford Hill, F.R.S.: Experimental Approach in Preventive Medicine—Influenza and the Common Cold (illustrated).
WILLESDEN GENERAL HOSPITAL MEDICAL SOCIETY.—At Department of Physical Medicine, 8.45 p.m., Mr. P. D. Trevor-Roper: Influence of Eye Disease on Pictorial Art.

Thursday, May 22

●CHARING CROSS HOSPITAL MEDICAL SCHOOL.—5.30 p.m., Huxley Lecture by Sir Howard Florey, F.R.S.: Changing Emphasis in Medical Research.
HONYMAN GILLESPIE LECTURE.—At Anatomy Theatre, University New Buildings, Edinburgh, 5 p.m., Dr. J. W. Farquhar: Child of the Diabetic Mother.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Epidemiology of Fungus Infections.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 3 p.m., Professor J. L. Wright (Otago): Exotics in Ectopics.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Professor O. L. Wade: Output of the Heart in Exercise.
ROYAL SOCIETY.—4.30 p.m., Croonian Lecture by Professor P. B. Medawar, F.R.S.: Homograft Reaction.
UNIVERSITY COLLEGE LONDON.—At Chemistry Theatre, Gower Street, W.C., 5.30 p.m., Inaugural Lecture by Professor D. McKie: Science and History.

Friday, May 23

HILL END HOSPITAL MEDICAL SOCIETY.—8.45 p.m., Dr. D. J. Williams: What Keeps us Conscious.
●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. S. C. Gold: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. W. P. Cleland: clinical demonstration.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 2 p.m., Mr. J. Hewitt: Variations on an Old Theme.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. Dillwyn Thomas: Some Observations on the Post-operative Care of Thoracotomy Cases.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Dr. J. D. Martin: Relief of Foetal Anoxia.

Saturday, May 24

SCOTTISH OTOLARYNGOLOGICAL SOCIETY.—At Royal Northern Infirmary, Inverness, 2.30 p.m., 76th meeting.

APPOINTMENTS

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—C. M. Jain, M.B., B.S., D.L.O., Registrar in Ear, Nose and Throat Surgery at South Devon and East Cornwall Hospital, Plymouth; G. W. Burgess, M.B., B.S., Surgical Registrar at Weston-super-Mare General Hospital; Joan J. Hudson, M.B., B.Chir., D.P.M., Assistant Psychiatrist at Horton Road and Coney Hill Hospitals, Gloucester; Mark Hewitt, M.B., B.S., M.R.C.P., Part-time Consultant Venereologist in West Cornwall Clinical Area; Jean M. Sheach, M.D., D.M.R.D., Consultant Radiologist in Exeter Clinical Area; J. E. A. Bartlet, M.D., M.R.C.P.Ed., D.P.M., Consultant Psychiatrist and Medical Superintendent at Exminster Hospital, near Exeter; W. Johnson, M.R.C.S., L.R.C.P., Registrar in Child Psychiatry and Mental Deficiency, Bristol.

BIRTHS, MARRIAGES, AND DEATHS

MARRIAGES

Keeler—Donaldson.—On April 30, 1958, in Nairobi, Kenya, Walter Richard Cubitt Keeler to Ann Kenya Donaldson (formerly Wilson).

DEATHS

Dunn.—On April 28, 1958, Wilfred James Dunn, O.B.E., M.B., B.Ch., Lieutenant-Colonel, R.A.M.C. (retired), of Shandon, Chorley Wood, Herts.
Fowell.—On April 28, 1958, at his home, Brackendene, Grayshott, Hindhead, Surrey, Patrick Harvey Clive Fowell, M.D.
Hibbert.—On April 28, 1958, at 13, Lower Brook Street, Ipswich, Suffolk, Wilfrid Lawrence Hibbert, M.R.C.S., L.R.C.P.
Jackson.—On April 22, 1958, Robert Best Jackson, O.B.E., M.D., D.P.H., of 21, Hazeldene Avenue, Bangor, Co. Down, late of Malaya and Hong Kong.
Kidd.—On April 27, 1958, Walter Shirley Kidd, M.B., B.S., of The Mount, Ingatestone, Essex, formerly of 4, Leeds Road, Harrogate, Yorks.
Manser.—On April 28, 1958, at Kent and Sussex Hospital, Tunbridge Wells, Kent, Frederick Bailey Manser, M.B., B.Ch., of 19, Calverley Park, Tunbridge Wells, aged 82.
Marshall.—On April 27, 1958, in London, William Porte Marshall, M.D., of Canada.
Monckton.—On April 28, 1958, at 9, Park Road, Ipswich, Suffolk, Robert Vernon Giraud Monckton, M.D., aged 80.
Pimm.—On May 4, 1958, at Bristol Royal Infirmary, Allan Pimm, M.R.C.S., L.R.C.P.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Paralytic Poliomyelitis in Infants

Q.—*Do infants under 1 year of age contract poliomyelitis in its paralytic form ?*

A.—Children under 1 year of age do contract paralytic poliomyelitis. In 1956[1] the number of paralytic cases for each year of age up to 14 was as follows:

Age	Cases
0–	45
1–	115
2–	134
3–	119
4–	123
5–9	422
10–14	173
Total	1,131

Four per cent. therefore of the total paralytic cases in children 0–14 years of age were in children under 1 year of age. Putting the information in another way, the number of cases in children below a year of age in 1956 was about one-third of the number in children aged 1, 2, 3, or 4 years, about one-half of the average number in children aged 5, 6, 7, 8, or 9 years, and about one and one-third times as many as the average number in children aged 10, 11, 12, 13, or 14 years. Paralytic poliomyelitis in children under 1 year of age therefore is not rare, and is probably slightly more frequent than the figures indicate owing to the difficulty of diagnosing it in some cases.

REFERENCE

1 *Registrar-General's Statistical Review of England and Wales for the Year 1956*, 1957, Part I, Tables, Medical, Table 32. H.M.S.O., London.

Crying and Redness of Eardrum

Q.—*Is it possible for excessive crying in a fractious child to cause engorgement of the eardrum ?*

A.—The short answer is "Yes." Just as crying in a child produces redness in the face from vascular engorgement, it would seem not unreasonable that the tympanic membrane should share in this reddening. But the reverse must be much more common—namely, that an otitis media is responsible for the crying. It is therefore important to decide whether the crying is causing the redness of the drum, or whether otitis media is causing the child to cry. The simplest way of deciding is by a careful appraisal of the tympanic membranes themselves. If they are merely flushed but still concave and mobile, and if they remain that way for 24 hours, there is probably nothing to worry about. But if the membranes lose their concavity and mobility, otitis media should be assumed. Mobility can readily be tested by attaching a Seigl type of rubber bulb to the speculum of an electric otoscope and gently blowing air in and out. The Seigl type rubber bulb is an extremely valuable piece of equipment. Many electrical otoscopes are fitted for its attachment, and it would be highly desirable if this became a standard practice.

Oral Vaccines

Q.—*What is the value, if any, of oral vaccines ?*

A.—Oral vaccines, particularly those against the enteric diseases, have been studied since the days of Pasteur. In man they are of no practical value, though some vaccines and also some toxoids do stimulate the production of a low level of antibody. The literature was well reviewed by Dolman,[1] and until recently there was nothing to be added to his survey; but it is now necessary to mention oral poliomyelitis vaccine. The ingestion of *living* attenuated strains of poliomyelitis virus has been shown in small preliminary studies[2] to stimulate the production of appreciable amounts of circulating antibody. Larger trials are at present being made. Unfortunately the strains used in the preliminary studies regain some of their virulence after passing through the human intestine. As poliomyelitis virus spreads widely in families and in other close-living communities, the question of the recovery of virulence of any strain used for vaccination is clearly of fundamental importance. An attenuated strain which became virulent might well start off a serious outbreak. It will be years before one can be certain of the stability of these attenuated strains, and it will therefore be years before oral poliomyelitis vaccination becomes common, even if it provides substantial protection.

REFERENCES

1 Dolman, C. E., *Amer. J. med. Sci.*, 1948, **215**, 327.
2 Dick, G. W. A., *et al.*, *Brit. med. J.*, 1957, **1**, 59.

Steroid Therapy and Resistance to Infection

Q.—*Is resistance to colds and other infections reduced during corticosteroid therapy ?*

A.—There is much experimental evidence that the administration of steroids to animals may lower their resistance to infection. The injection of small amounts of cultures of living organisms, which caused only local and transient symptoms in untreated animals, was followed by septicaemia and death in animals given relatively large doses of cortisone. In practice, however, there is little evidence that patients on the low maintenance doses of cortisone or of the newer analogues, prednisone and prednisolone, now used in diseases such as rheumatoid arthritis, are more susceptible to colds or other infections, or that the signs of such infections are suppressed. In more serious conditions, such as systemic lupus erythematosus or polyarteritis nodosa, where much larger doses may be necessary for control of symptoms, the risk is greater. Such patients need close supervision. They should be instructed to inform their doctors should new symptoms appear, no matter how trivial. Infections should be treated promptly with an appropriate antibiotic. Steroid therapy should never be stopped suddenly because of a complicating infection, in view of the serious risk of a severe exacerbation of the condition under treatment. In fact, the maintenance dose should be increased temporarily to tide the patient over the period of increased stress.

Skin-cleansing Agent

Q.—*What is a suitable skin-cleansing agent for minor surgical procedures ?*

A.—Although this may seem a simple matter, it has been the subject of prolonged controversy, and no simple answer to the question would command universal agreement. The object is to destroy the "transient" flora of the area, and in circumstances precluding prolonged preparation of the skin a rapidly acting germicide is required. Such slowly acting substances as mercurials, acridine compounds, and other dyes are therefore quite unsuitable. It is almost universally agreed that tincture of iodine is the most effective rapid germicide for the surface of the intact skin, but there are objections to its use, the chief of which is that some skins are sensitive to it. Some of the controversy in recent years has centred on the relative merits of alcohol and of quaternary ammonium compounds. The evidence is much in favour of the former. Story,[1] for instance, found that alcohol destroyed pathogenic staphylococci on the skin much more rapidly than did cetrimide. The latter was indeed only effective under the conditions of this test when in alcoholic solution. A satisfactory solution is therefore 75% of spirit, or, if the detergent and cleansing action of a quaternary is considered an added advantage, 1% cetrimide in 75% spirit. A relative newcomer to this field, and a powerful germicide, is chlorhexidine ("hibitane"), the skin-disinfecting properties of which have naturally not been studied as thoroughly as those of older germicides.

This is commonly used in 0.05% solution also containing 0.5% of cetrimide. Any of these solutions can be coloured with an inert dye if desired.

REFERENCE

1 Story, P., *Brit. med. J.*, 1952, **2**, 1128.

Morphine for Haemorrhage

Q.—*What is the chief reason for giving morphine for haemorrhage?*

A.—The chief reason for giving morphine when haemorrhage has occurred is that it has been found to diminish the risk of shock. This was the experience of those treating air raid casualties during the last war. The patient who has lost blood becomes anxious and restless and the pulse may become imperceptible. Morphine helps to minimize these ill effects.

Recurrent Bladder Papillomata

Q.—*What treatment, other than repeated diathermy, is there for recurrent multiple papillomata of the bladder?*

A.—As with every other condition, diagnosis must come before treatment, and the complete diagnostic procedure for recurrent papillary tumours of the bladder includes a cystoscopic biopsy and an excretion pyelogram. The former is necessary for determining the grade of malignancy of the tumour, as many so-called papillomata are in fact papillary carcinomata. If they are of a higher grade than a papillary differentiated tumour they may require irradiation for their satisfactory treatment. Supervoltage *x*-ray therapy for this condition is on trial, but in certain cases total cystectomy is the only curative procedure. An excretion pyelogram is necessary to make sure that there is no primary papillary tumour in the kidney, for if there is the bladder tumours will continue to recur whatever the treatment. In many cases the disease must be regarded as one which affects the whole bladder, and treatment must be applied accordingly.

Genetics of Longevity

Q.—*Have there been any studies carried out on the genetics of longevity?*

A.—Yes. Extensive family studies were made by Professor Raymond Pearl.[1] More recently twin studies have been reported from America and Germany.[2 3] The family studies show a definite tendency for longevity to run in families. Both the parents and children of long-lived individuals have themselves an increased expectation of life. The twin studies show a tendency for the intervals between the deaths of monozygous twin pairs to be less than that between the deaths of dizygous pairs of like sex. The mechanism of genetic determination of longevity is not known, but is likely to be multifactorial.

REFERENCES

1 Pearl, R., and Pearl, R. D., *The Ancestry of the Long-Lived*, 1934. Baltimore.
2 Kallman, F. J., and Sander, G., *J. Hered.*, 1948, **39**, 349.
3 Koch, C., *Act. Genet.*, 1957, **7**, 47.

Iron in Wine

Q.—*Which wines contain the highest proportion of easily assimilable iron?*

A.—Iron in wine comes from two sources, that present in the grapes and that introduced from the metal parts of the presses used in pressing the grapes. The greater part of the large amount of iron that may be introduced during pressing is precipitated and removed in the racking process during fermentation, but the amount remaining in solution may still be larger than that originally present in the grapes.

The concentration of iron in a wine depends primarily on the method and care used in pressing. In general, when great care is used and the grapes are treated very gently at all stages the wines—for example, champagne and sparkling wines—tend to contain the least iron, whereas when less care is necessary—for example, in making red wines—the product contains more. The range in wines normally consumed in this country is from 0.2 to 2.0 mg. Fe per 100 ml. The iron is present in the form of soluble salts of organic and inorganic acids and is probably as readily assimilable as most medicinal preparations of iron.

NOTES AND COMMENTS

Obstetric Prognosis after Fractured Coccyx.—Dr. LOGAN MITCHELL (Leicester) writes: Your reply on the prognosis in fractured coccyx in labour ("Any Questions?" April 5, p. 843), which ends with the dogmatic statement that "the coccyx will not obstruct labour," cannot go unchallenged. I remember as a houseman having to enlist the aid of the registrar in performing a low-cavity forceps delivery on an elderly primipara. I had employed what I thought to be a reasonable amount of force, without producing the slightest degree of descent. The registrar then removed the blades and made a further vaginal examination. He was satisfied by what he found, reapplied the blades, and exerted traction. The head stayed firm, and the obstetrician's distress became marked. Desperation succeeded wisdom in the traction force employed, and with a crack like the one o'clock gun delivery was effected. The registrar, paler than he was at the beginning of the operation, did another vaginal examination, and felt the now-mobile tip of coccyx protruding into the posterior vaginal wall. There was an obvious furrow on the baby's head, where it had met the obstruction. I questioned the mother afterwards and elicited the not uncommon history of her having fallen across a wooden chair some twenty years previously. May I be equally dogmatic and say that the coccyx *will* obstruct labour?

OUR EXPERT replies: The experience described by Dr. Mitchell is by no means uncommon. Although it may appear to contradict the sentence quoted, this is only because the words are taken out of their context. The original question and answer were concerned with fracture of the coccyx sustained during a previous labour. The sentence quoted applied to a specific case in which vaginal delivery had already been accomplished in the past. The circumstances described by Dr. Mitchell are different. Even in these, however, it can still be said that the coccyx does not, *by itself*, offer an insuperable obstruction to delivery. If it will not bend backwards, it can be deliberately fractured or mobilized digitally without significant ill effect—provided the cause of the dystocia is recognized.

Daily "Drinamyl."—Mr. L. W. REID (Science Information Department, Smith Kline and French Laboratories Ltd., London, S.E.5) writes: The answer to this question ("Any Questions?" April 12, p. 902) may be misleading. The answer was, "It is difficult to envisage any harm arising from the daily administration of a single tablet," but the patient was warned against increasing the amount taken. Surely this should have been "without advice from her doctor." One tablet of drinamyl daily is quite a small dose. It is universally given at much higher doses with perfect safety, but, of course, only on the doctor's advice.

Corrections.—We are grateful to Miss WINIFRED FERRIER for pointing out two mistakes in our note about the Kathleen Ferrier memorial at University College Hospital (*Journal*, May 3, p. 1075). She writes: "First, it was not my sister's idea that a memorial fund should be established. What she said was that *when* she got better she would give a concert for the benefit of the hospital. Second, my sister had no throat ailment whatever."

We erred in stating (May 10, p. 1126) that the late Mr. Gerald Robinson was a widower at the time of his death. Mr. Robinson's first wife died in 1955 and he married again in the following year. He is survived by a widow and by a son and a daughter of his first marriage.

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